MANAGING MAINTENANCE COSTS OF PHARMACEUTICAL RESEARCH AND DEVELOPMENT

By

Jared Butts

B.S. 2002, Mechanical Engineering, Brigham Young University
M.S.E. 2003, Naval Architecture and Marine Engineering, University of Michigan

Submitted to the MIT Sloan School of Management and the Engineering Systems Division in Partial Fulfillment of the Requirements for the Degrees of

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AND
Master of Science in Engineering Systems

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Signature of Author _____
May 8, 2009
Engineering Systems Division, MIT Sloan School of Management

Certified by _____
Daniel Whitney, Thesis Supervisor
Senior Research Scientist, Engineering Systems Division

Certified by _____
Roy Welsch, Thesis Supervisor
Professor of Statistics and Management Science, Dir, CCREMS, MIT Sloan School of Management

Accepted by _____
Nancy Leveson, Chair, Engineering Systems Division Education Committee
Professor of Aeronautics and Astronautics and Engineering Systems at MIT

Accepted by _____
Debbie Berechman
Executive Director of MBA Program, MIT Sloan School of Management

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Managing Maintenance Costs of Pharmaceutical Research and Development

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ABSTRACT

Drug Discovery is a race to be the first to patent a drug that meets a significant medical need in the world. Many pharmaceutical companies are now using automation extensively to improve consistency and aid personnel in testing the millions of potential drug candidates within their labs. Because these machines play an important role in drug discovery, there is significant interest in managing their maintenance. The concern is that downtime is hampering the efforts of drug discovery.

This project has sought to reduce that downtime and manage maintenance costs by working with the Technical Operations Group, Novartis' in-house maintenance team. The main objectives have been to devise a better way for evaluating maintenance contracts, improve the availability of the equipment, and instill a culture of continuous improvement in the group.

This study shows that maximizing equipment utilization should be a higher priority than reducing downtime. The data show that the high throughput systems are only used an average of three days a week. Reducing downtime, which is most often measured on the scale of minutes, is unlikely to bring about the gains that would be realized by improving capacity utilization. Current metrics and data collection procedures are ineffective for determining automation needs and performance as well as engineer performance. A new system for data collection was implemented along with improvement projects as an introduction to lean principles, with the primary objective being a self-sustaining system of finding process improvements. Contracts were evaluated along four criteria: the indispensability of the equipment under contract, the adjusted replacement cost, the level of customization, and the age of equipment.

The end results of the internships include a metric gathering system that more closely monitors engineer activity as opposed to equipment activity, completed improvement projects such as the complete overhaul of the tool room including inventory management as well as an automated error log system, and a way of evaluating contracts that will reduce costs without sacrificing performance.

Thesis Supervisor: Roy Welsch
Title: Professor of Statistics and Management Science, Dir, CCREMS, MIT Sloan School of Management

Thesis Supervisor: Daniel Whitney
Title: Senior Research Scientist, Engineering Systems Division

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GLOSSARY

Assay: A qualitative or quantitative biochemical experiment that tests the efficacy or potency of a drug candidate with a biological substance

Engineer: NIBR associate responsible for maintenance and repair of automated equipment

- Generally have engineering or other technical background

Hit: A chemical substance that shows activity on a selected biological entity (target) and is shown to have the correct identity and acceptable purity

HTS: High Throughput Screen

- An assay that is scaled to handle multiple plates and multiple chemical and biological substances (100, 000 -> 1,000,000)
- NIBR has three HTS systems, with HTS-3 being able to handle plates with a smaller well-size (1,536-well plates)

LFP: Lead Finding Platform

- Division within NIBR responsible for Lead Discovery

MTBF: Mean Time Between Failure

- The average time between failures of a system
- It is the sum of the operational periods divided by the number of observed failures
- A high value is desirable

NIBR: Novartis Institutes for BioMedical Research

Plate: Industry-wide standard rectangular plastic grid containing small wells that store the chemicals for testing or act as reaction vessels during testing

- They have an area the size of an index card
- Plates usually contain 386 or 1,536 wells
- Most automation in the lab is designed around handling these plates

QC: Quality Control

- Calibration performed at the beginning of an experiment to ensure equipment is operating as expected

Screener: The NIBR scientist that develops the assay and then runs the integrated equipment

- Have biology background
- LFP has about 25 screeners that were associated with this study

SolAr: Solution Archive

- Automation system that stores compounds in liquid form under refrigeration
- Prepares plates by loading the wells with the compounds for use in other systems like HTS

Target: A native protein whose activity can be modified by a chemical substance resulting in a desirable therapeutic effect

TechOps: Technical Operations Group

- Team consists of five engineers and one supervisor
- Responsible for maintenance of automated equipment within the Lead Finding Platform

INTRODUCTION

1 Case study

The basis for this research is a case study of the maintenance group within a large pharmaceutical company, in this case Novartis. The author spent six months onsite working with the maintenance engineers to examine current methods for handling the care of automated equipment. This research is a result of the observations and interviews while onsite as well as a review of the most current literature on pharmaceutical maintenance.

1.1 Company background

In 1996, Sandoz and Ciba-Geigy joined to form Novartis. Based in Basel, Switzerland, Novartis is a global leader in innovative pharmaceuticals, generics, vaccines, and consumer health products. Research into new pharmaceuticals at Novartis is conducted primarily through the Novartis Institutes for BioMedical Research (NIBR). Headquartered in Cambridge, Massachusetts, with locations worldwide, NIBR is committed to discovering innovative medicines to address unmet patient needs.

The Lead Finding Platform (LFP) division at NIBR is a key part of the Drug Discovery process. It contributes to the discovery of novel medicines through testing of large numbers of small molecules against a target to find Hits, as done in high-throughput screening (HTS), and determining a chemical's action on many different targets, as done in selectivity or safety profiling. Both screening and profiling currently use a high degree of automation as well as numerous assay and information technologies.

Within LFP at the Cambridge, MA site is the technical operations group, or TechOps. This group, consisting of five engineers and one manager, is responsible for the repair and maintenance of the automated equipment.

1.2 Statement of problem

Drug Discovery is a race to be the first to patent a drug that meets a significant medical need in the world. Some of these drugs can bring in over $1B in revenue per year, so there is significant competition and effort centered around getting drugs to market quickly and having them protected by patents for as long as possible. However, taking a drug from concept to market is a long, arduous process that involves multiple test phases and takes around 12-14 years to complete. Patents typically last around 20 years, so the longer it takes to get the drug to market, the less time there is to recoup drug development costs and turn a profit.

To facilitate the discovery process, many pharmaceutical companies are now using automation extensively to improve consistency and aid personnel in testing the millions of potential drug candidates within their labs. Because these machines play an important role in drug discovery, there is significant interest in managing their maintenance.

At NIBR, automation is used for the preparation, processing, testing, and storage of compounds (potential drug candidates), reagents or tools (proteins or cells). Due to the nature of the research, these automated machines are asked to perform a different task for every screen, whether it be performing operations in a different order or changing the operations themselves. The automated equipment at NIBR can shut down, often due to the slightest problem. This is related to many things including the complexity of the equipment and the variation of the experiments performed on the equipment.

These system shut-downs have led to a reluctance of the operators, known as the "screeners" in this study, to run the automation overnight. A survey taken of all automation screeners showed that 80% of those responding felt that reliability concerns have "some" to "great" effect on their decision to run equipment overnight. The full results of the survey are given in Appendix A. Though the equipment is perfectly capable of running unsupervised, there is no one around overnight to respond to a shut down. This situation either requires the screener to come in to work in the middle of the night to try and fix the issue, or allow the time-sensitive materials being tested to go to waste. To avoid having to make that decision, screeners prefer not to run the automation

overnight, resulting in an underutilization of capacity. If the screens were run, or capable of running, unsupervised, the length of many screens could be cut in half savings weeks or months of screen time.

To help reduce the downtime, NIBR has a small group of engineers known as the Technical Operations Group, or "TechOps". TechOps is responsible to maintain and repair all of automated equipment within the Lead Finding Platform (LFP). TechOps is able to respond to equipment failure quickly, though only during the day, and they often find themselves "firefighting" without getting to the root cause of the failure. In addition, some failures, such as proprietary custom software on the more complex and integrated pieces of equipment, are beyond the capability of the group to fix. To handle this issue, LFP has a number of maintenance contracts with the equipment manufacturers to diagnose and repair those issues that currently can't be handled in-house by TechOps.

The recurring equipment problems, expensive maintenance contracts, and "firefighting" culture all indicate there could be significant waste in the system. Without appropriate metrics to gauge performance or progress and without a good understanding of automation capacity and capability, LFP is seeking to better understand how to improve both automation and maintenance performance.

1.3 Purpose of study

The purpose of this study is to analyze the decisions and procedures used in the maintenance of drug discovery automation and to make recommendations as to how to best manage the costs thereof. This analysis will center on a case study in the form of NIBR, a drug discovery center that uses automated equipment that is relatively common to the industry. A secondary purpose of the study is to make some analysis of the purchase and use of the automation itself.

1.4 Summary

It should be mentioned that not all pharmaceutical research centers operate in the same way. In fact, even among Novartis research centers there are noticeable differences. This case study is not

meant to imply that NIBR is the norm or representative of most pharmaceutical companies. Most companies will differ somewhat in regards to what vendors they use and the degree to which they utilize automation. Some may use different technologies than those of NIBR. Some companies may even use a staff dedicated solely to running the automation. However, the author considers it reasonable to assume that there are principles discussed in this study that can be applied to a number of other organizations, and it is up to the reader to make those analogies that will be most applicable to his or her own situation. Chapter 2 discusses the process and problems associated with drug discovery and its maintenance as it applies to NIBR.

2 The Pharmaceutical Research Environment

The pharmaceutical research environment is much like other life-science research environments. Researchers in white lab coats are seemingly working independently on a variety of projects. Surrounding these scientists is a variety of equipment, supplies, and various chemicals. NIBR may be working on different projects or using different equipment than other pharmaceuticals, but the basic process of drug discovery is essentially the same.

2.1 The Drug Discovery Process

The drug development process is a long one, often taking 10-14 years from concept to market. These drugs pass through multiple phases of testing, and thousands of drug candidates are tested for every drug that makes it to the market. The first portion of this development process is referred to as drug discovery. From the Novartis website:

> "All drug discovery efforts at the Novartis Institutes for BioMedical Research (NIBR) focus on patients. Scientists determine which diseases will be the focus of research efforts based on two questions: Do we have or can we gain significant understanding of the cause or "mechanism" underlying the disease, and does this disease represent a significant unmet medical need? If the answer to both questions is yes, then NIBR develops a research program aimed at better understanding the disease and finding an effective therapy. Early discovery science determines how a disease is caused at the molecular level, using our own discoveries as well as those from collaborations with scientists at several institutions. We look for clues in both the patients' experience of the disease and the compendium of medical knowledge assembled over centuries, integrated with the growing knowledge of human biology and genetics.

Target and compound selection

Traditional pharmaceutical development relies heavily on identifying appropriate drug "targets," such as single genes or proteins. As our knowledge of human biology has grown,

so has our understanding of what we mean by targets for drug discovery. We now understand that a target may be entirely interacting pathways of proteins, which in turn can be at the root of several different and seemingly unrelated diseases. As a result, NIBR scientists concentrate their efforts on discovering and inventing compounds that can alter the disease-causing mechanism, whether a single protein or a complex pathway of proteins, to bring it back in line with normal function.

Target validation and compound optimization

When a suitable target and compound are identified, the targets are rigorously "validated," or proven to be involved in the disease state, and the compounds are "optimized," altered in ways that both increase their efficacy and minimize any potential side effects. The tools of modern chemistry and biology merge in these stages to give us the best candidates for drugs of the future.

Proof-of-Concept trials

Following validation and optimization, it is critical to test both the compounds and the identified mechanisms or targets in actual patients before full development. Bridging the lab and the clinic with experts from both sides, NIBR scientists work closely with Development to perform Proof-of-Concept (PoC) clinical trials. These trials, performed with a small number of patients, aim to provide initial data about the efficacy and safety of the chosen compound, and validate our understanding of the relevant mechanism." (1)

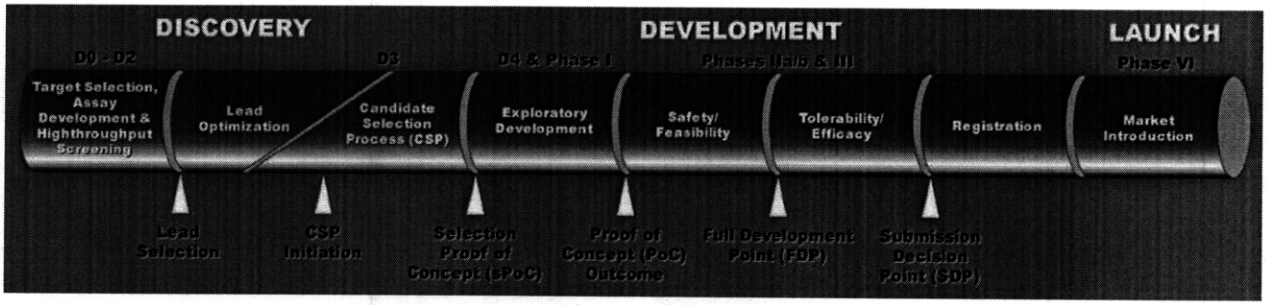

Figure 1. Drug Discovery and Development Timeline

A timeline of this process is shown in Figure 1. This study is solely involved with the target and compound selection portion of this process, and only those operations that involve the services of the TechOps group. The target selection and assay development process often take up to a year. When the assay is ready, it moves on to high throughput screening. It is at this phase where most of the larger automation equipment starts to be used, so that is where this study will focus. The basic process involves taking the target, usually a certain type of cell or protein, and preparing it to be exposed to hundreds of thousands of chemical samples. These samples, contained in plates, are then tested to see if a desired reaction has taken place. Those compounds that produce the most desirable reactions are further tested to validate the results, determine the most advantageous concentration and potency, and check for purity and identity. Only those compounds that pass these tests will be passed along by NIBR for further evaluation as potential early drug candidates.

2.2 Automation at NIBR

The automation under the umbrella for which TechOps is responsible to maintain consists of four major areas: plate preparation, tool production (protein or cellular), drug discovery screening, and toxicology screening. Tool production wasn't considered for this study. The majority of this equipment involves moving plates around, dispensing minute volumes of liquid (usually on the scale of micro- or nano-liters), reading plate "results", or a combination of the three. Among the other, more specialized, equipment NIBR has includes equipment involved with incubation, stirring, and shaking of the compounds and reagents.

It is important to point out that there are two "levels" at which automation is used at NIBR. As technology has advanced, the screener has less and less manual involvement with the assays. Previously, manual liquid dispensing and testing were replaced by stand-alone systems that could, for example, measure out specified volumes of liquids into plates and stack the plates in preparation for the next operation. The screener was still responsible to load and unload the plates, possibly in a time-sensitive manner. This equipment, which generally has a footprint no greater than that of a tube television, sits on a benchtop and is thus referred to as benchtop equipment. The term "automation", however, more commonly refers to that equipment that can combine multiple operations without user intervention. These systems essentially consist of multiple benchtop units that interface with one another via robotic arms, conveyor belts, and specialized software. The

automation "systems" generally take up the space of a very small room and are significantly more expensive and difficult to maintain. Importantly, all the integrated systems have custom software that couples all the components together to function as one. This software can represent up to 30% of the total cost of the system and can be difficult to modify as the code is often proprietary to the vendor.

Both benchtop equipment and automation systems accomplish the same tasks and do so by replacing some level of human involvement, and thus both can be considered "automation". NIBR still has significant benchtop capacity, partially to handle smaller assays and partially as a backup to the bigger systems. One of the major differences, though, is that the larger systems are designed to be flexible in what they accomplish. Couple this with a variety of users, and the result is a very non-standardized process. Automation, like other technology, usually settles into what's known as the "bathtub curve" as shown in Figure 2. This curve shows how the number of equipment failures drops as the "bugs" are worked out during set-up, after which the equipment settles into a constant failure rate. At the end of its service life, the equipment tends to wear out more and the failure rate climbs back up.

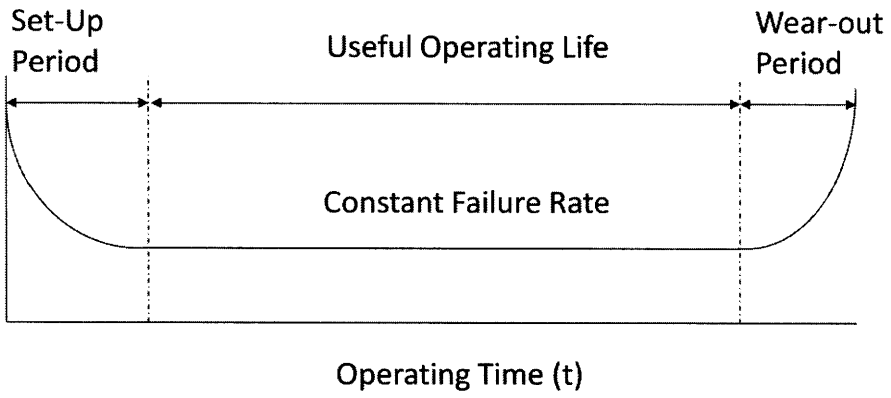

Figure 2. Typical Bathtub Curve

However, the "bathtub" curve more accurately represents equipment that has standardized processes. In the world of pharmaceutical R+D, there are few standardized operations. At NIBR, even the users of the equipment change on a weekly or monthly basis. By its very definition,

"research" implies doing things that haven't been tried before, and thus some increase in failure rate is likely. A more typical result for R+D automation's service life may look like Figure 3. Each peak in the "useful operating life" represents a different screen that is usually characterized by a high initial failure rate. In this case, most of these failures aren't the result of a physical part breaking or wearing out. These failures are any occurrence that causes the system to be unavailable. It could be that the system "can't find" a plate, meaning either that the robotic arm wasn't programmed correctly, the plate wasn't put in correctly by the user, the plate fell off at some point during the process, or there is a glitch in the software that had never been worked out because the system had never been used in such a way. Often, these failures are software-related. Perhaps just as often, simply pushing the "restart" button will get the system operating again with no problems. But it could very well be the case that the user could prevent the majority of these software errors. For example, a common error according to the data is the improper start-up or shut-down of a piece of equipment within a system. The individual impact of such an error is small, but how many times does it have to happen to be worthy of attention? The bottom line is that there is no system in place to ensure that the same error doesn't happen again.

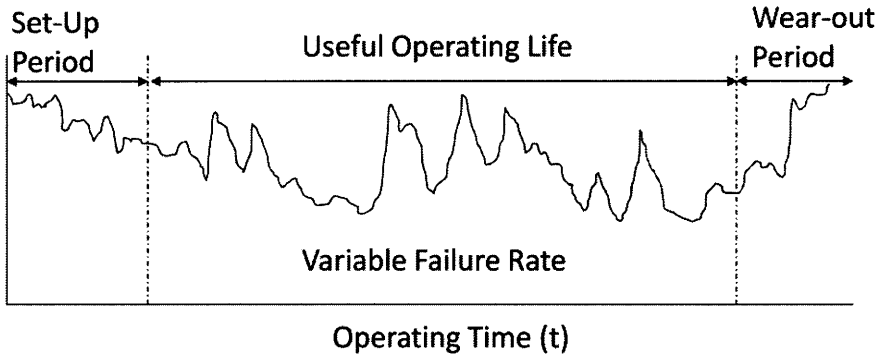

Figure 3. "Random" Error Performance

2.2.1 Sample Preparation in Plates

Before assays can be run, a set of plates containing the compounds has to be prepared. NIBR has over a million compounds in its library. These compounds arrive at NIBR in bulk-solution form from the Basel site in tubes and master plates, and then are stored in refrigerated storage for up to three years, at which point they are replaced or replenished. These compounds comprise what

NIBR considers to be the most likely set of compounds from which drugs can be produced. To help with the storage and distribution of these compounds, NIBR uses an automated system referred to as Solar, which stands for "solution archive". Solar includes the refrigerated storage library, as well as a series of robotic arms, conveyor systems, and liquid dispensers. When a screener has an assay ready to be screened, he or she will request either the entire library of compounds or some subset of the library against which to test. As the numbers of compound samples is so large, Solar is set up to "stamp" out, or replicate, copies of the library or sub-library from its master solution plates (384 wells at a time) and dispense a few micro-liters of the solution into new destination plates. These plates, all of a standard footprint about the size of an index card, contain either 384 or 1,536 wells. The trend has been to use smaller and smaller quantities and thus use plates containing more wells, but not all testing equipment is capable of handling the higher density plates. Pictures of the Solar system are shown in Figure 4 and Figure 5.

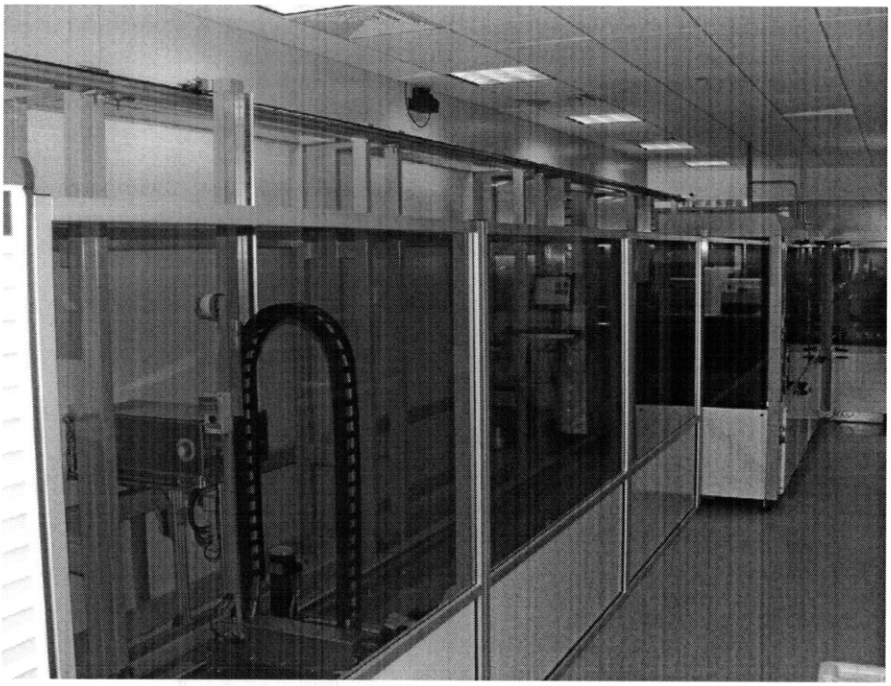

Figure 4. Exterior of Solar automation

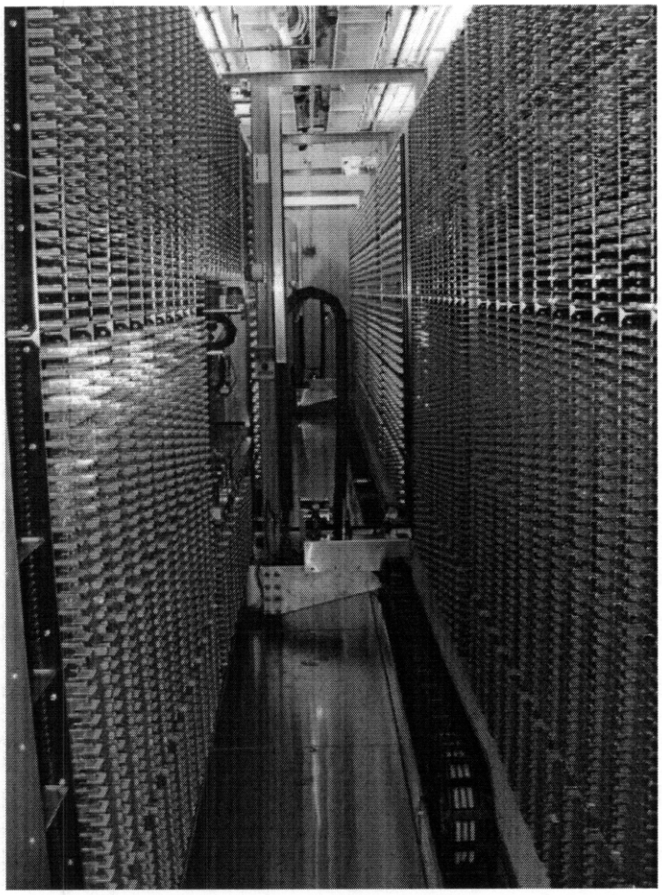

Figure 5. Interior of Solar automation- the refrigerated compound library

In addition to making copies of the full library, the Solar system will also pick out certain compounds upon request from its larger volume tube store. Here, rather than arraying compound solutions in 384-well plates, each compound solution is available as an individual tube. Picking individual solutions is usually the case after a full screen is run and the screener wants to focus on and further test the most promising compounds. This often involves not only selecting specific compounds, but putting those compounds in multiple wells at different concentrations. The selection of specific compounds is referred to as "cherry picking" and can be a very time consuming process.

The Solar system is one of the few that will be run on a regular basis overnight, as it can take days to create a copy of the entire library. NIBR keeps up to six full copies of the library already plated and stored under refrigeration to be ready at any time. The group that uses this equipment is the compound management unit, or CMU, and they tend to maintain the system on their own. That is

to say, they don't use the services of the TechOps group as much as some other divisions. Solar has a group dedicated specifically to its operation and thus its operators have a higher level of familiarity with the system. In addition, Solar's processes are more standardized than many of the other systems. However, they still use contract maintenance from the equipment vendor fairly often. This is partially due to the fact that TechOps isn't as familiar with the system, the software is complex and proprietary, and there is little redundant capacity to handle plate preparation if the system goes down.

At the end of the case study, the CMU had purchased another system, known as HARP that prepares plates through acoustic dispensing. Instead of transferring compound solution by pipetting, the HARP holds an empty plate upside down above the compound solution, and then an acoustic signal is sent from underneath the solution, "flicking" a small droplet of the fluid through the air up onto the surface of the empty plate, where it is held in place by surface tension. The advantage of this system is it can populate the plate wells a lot faster than Solar. However, at the time of this study's end, this system was not yet functional, as even brand new components needed to be replaced. More will be said about automation purchase decisions later in the study.

2.2.2 Drug Discovery Screening

NIBR has a number of different systems involved in drug screening. This equipment falls under the direction of the hit discovery group, or HDG. In addition to the aforementioned benchtop equipment, NIBR has three high throughput screening systems, known as HTS-1, HTS-2, and HTS-3. These systems require that the screener load in their set of plates and the kinds of reagents they would like to use, and then, with TechOps support, programs the equipment to move, process, incubate, and read the plates.

Within each HTS system are pieces of equipment from different vendors that have to "talk" to one another. To do this, separate software known as Polara was designed by the vendor to coordinate the efforts of these systems. Running a screen consisting of the full library of plates can take anywhere from one to four months on average. HTS-1 and HTS-2 are very similar systems with similar capabilities. The HTS-3, the newest of the systems, can handle the 1,536-well plates and thus

can has the ability to process the full library of plates much faster than the other two systems. Pictures of the HTS systems are shown in Figure 6, Figure 7, Figure 8, and Figure 9.

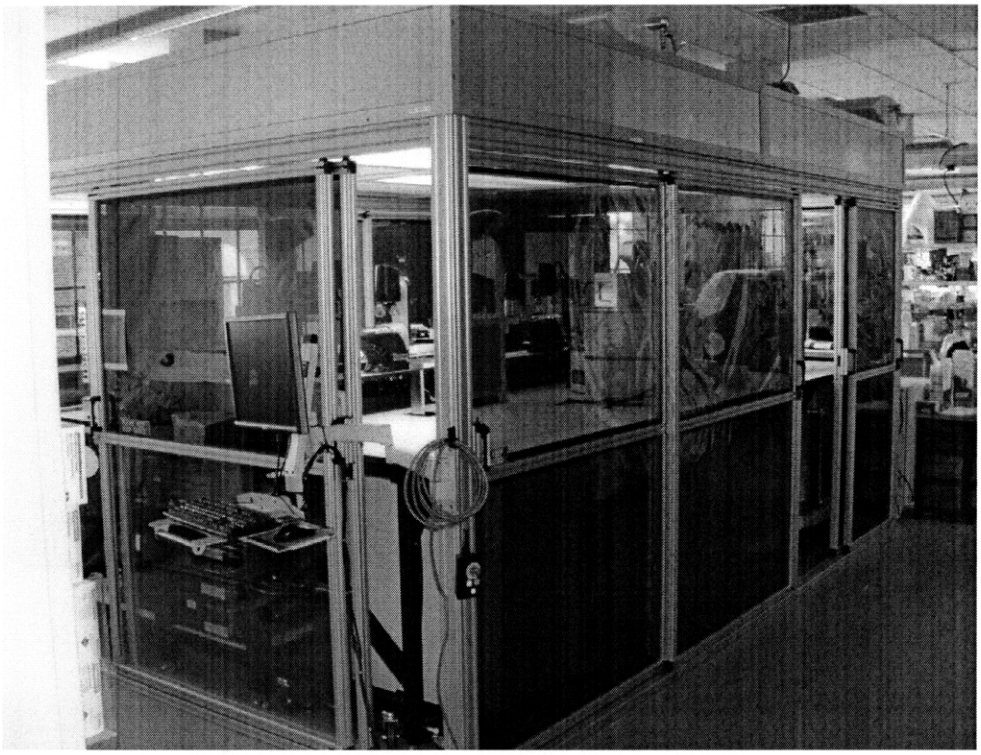

Figure 6. Exterior of HTS-1 (similar to HTS-2)

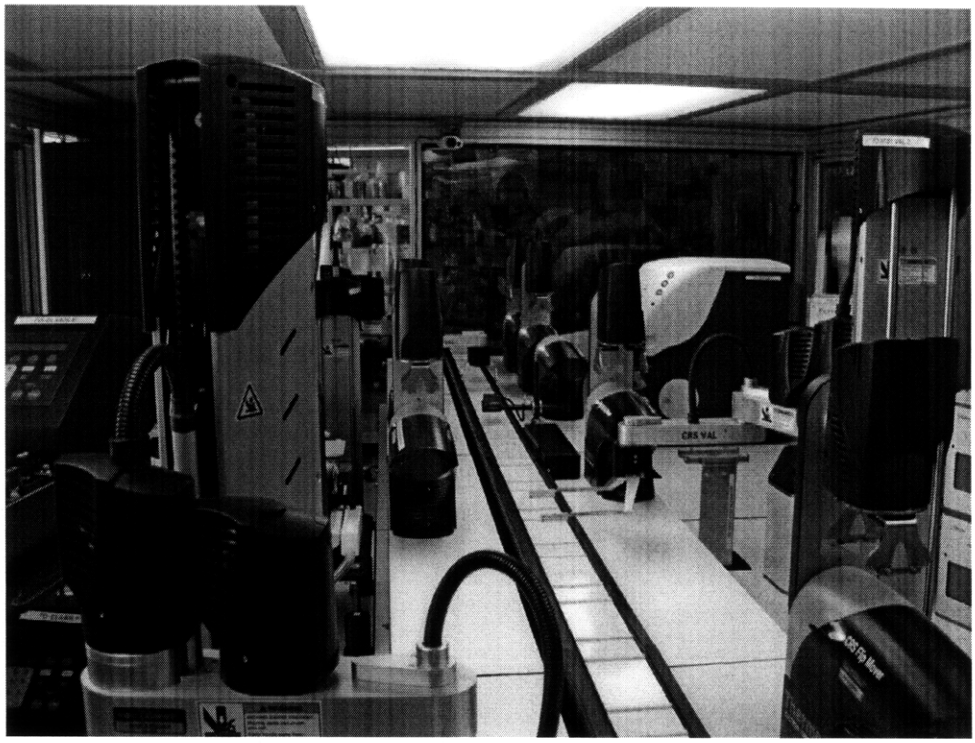

Figure 7. Interior of HTS-1 (similar to HTS-2)

Figure 8. Exterior of HTS-3

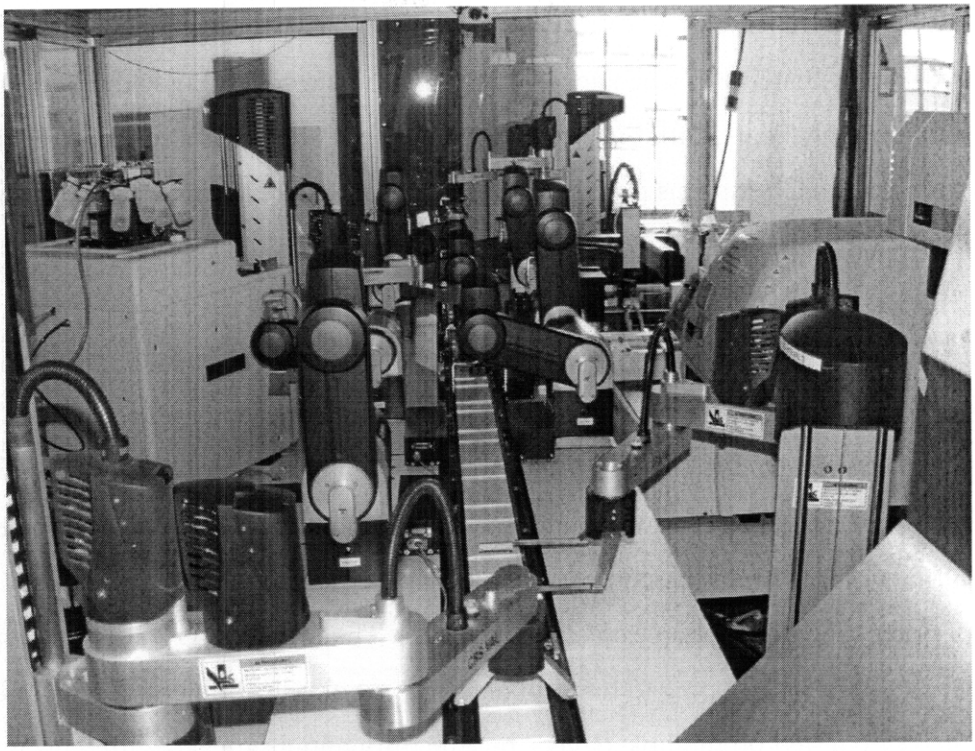

Figure 9. Interior of HTS-3

Of all the equipment that TechOps services, the HDG's equipment, both benchtop and fully automated, gets the most attention. There are a few reasons for this. First of all, HDG represents the largest group, both in terms of numbers of screeners and amount of equipment. Second, HDG has the least standardized procedures of the three groups under consideration. Every time a screen is run, the equipment is being asked to perform a slightly different task, be it the order of operations, the incubation time, the reagents used, etc. Performing different tasks also leads to reprogramming the HTS systems for every screen, which leads to additional sources of error. Finally, the HDG equipment simply has the most problems. This is related to the fact that there are so many pieces of equipment that perform different functions, but also to the fact that sometimes this equipment can sit idle for weeks or months, which generally has a negative effect on the equipment. (2) Also, unlike the other two groups, each screener only uses the equipment a few months out of the year, making it harder for them to stay up-to-date on how to properly use the systems.

The HDG has a goal of 20 screens per year across the three HTS systems. To the author's knowledge, this goal has not been achieved in the past. However, the HTS-3 system was only about a year old at the time of the study. Scheduling has also been a very difficult aspect of trying to reach

this goal. Screeners can spend a year or more developing the assay in preparation for screening. This produces some variability in when an assay is going to be ready. Couple this with the fact that an HTS system can only be used for one screen at a time, and HDG has a situation in which there are more screens than HTS systems just as often as there are HTS systems sitting idle for weeks at a time.

2.2.3 Toxicology Screening

The final group that TechOps supports is the preclinical safety profiling group, or PSP. Whereas the HDG group was testing a target, be it a type of cell or a biochemical substance, against multiple compounds, the PSP group tests a compound against multiple targets. Unlike HDG, the work PSP does has a different focus and is based on early safety assessment. The tests PSP do may be the first indication of potential toxicity of an early drug candidate. Thus, in the HDG they are hoping for hits, but in the PSP they are hoping to have no hits. PSP is not only differentiated from HDG in that compounds are tested on multiple targets, but the throughputs are very different. While HDG can test a million compounds up to 20 times per year, the total number of compounds tested by PSP could be only a few thousands per year in total. The integrated systems the PSP group uses are consequently different from HDG's.

The main automated system within this group is known as the P-5 system. P-5 only has two or three users and runs a fairly stable process. A picture of the P-5 system is shown in Figure 10. In addition, this system is only used every other week. P-5 is capable of handling more work, but due to the high costs of the target materials used, management limits the number of toxicology screens run per year. Because of these factors, TechOps does not receive a lot of service calls on the P-5 system.

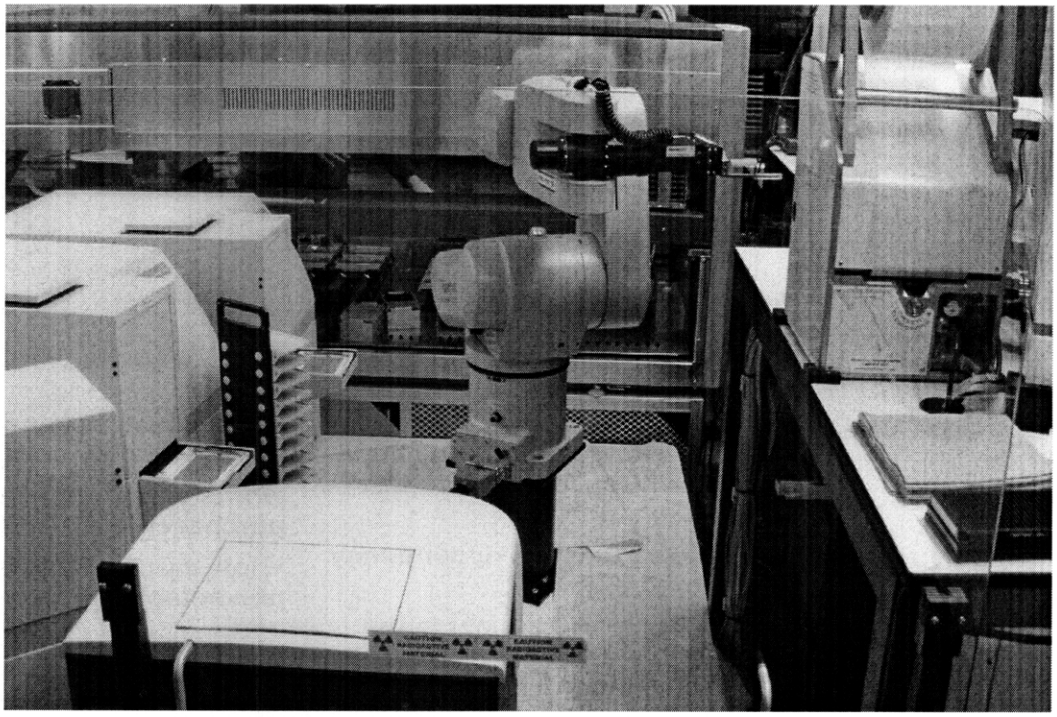

Figure 10. The P-5 system

2.3 Maintenance Costs

NIBR doesn't have a central group that manages all maintenance costs, but TechOps certainly has the power to influence all maintenance costs associated with the equipment that they service. There are a number of areas associated with maintenance that have costs associated with them including the opportunity costs of maintenance. For this study, the costs have been separated into the following categories: downtime costs, maintenance contracts, and parts and service calls, as shown in Figure 11. Note that this does leave out the TechOps salaries as part of the cost of maintenance. In reality, these costs would also play into management decisions about maintenance costs. However, the author feels it is more beneficial to learn how to maximize the benefits of the resources in place before considering adding or removing resources.

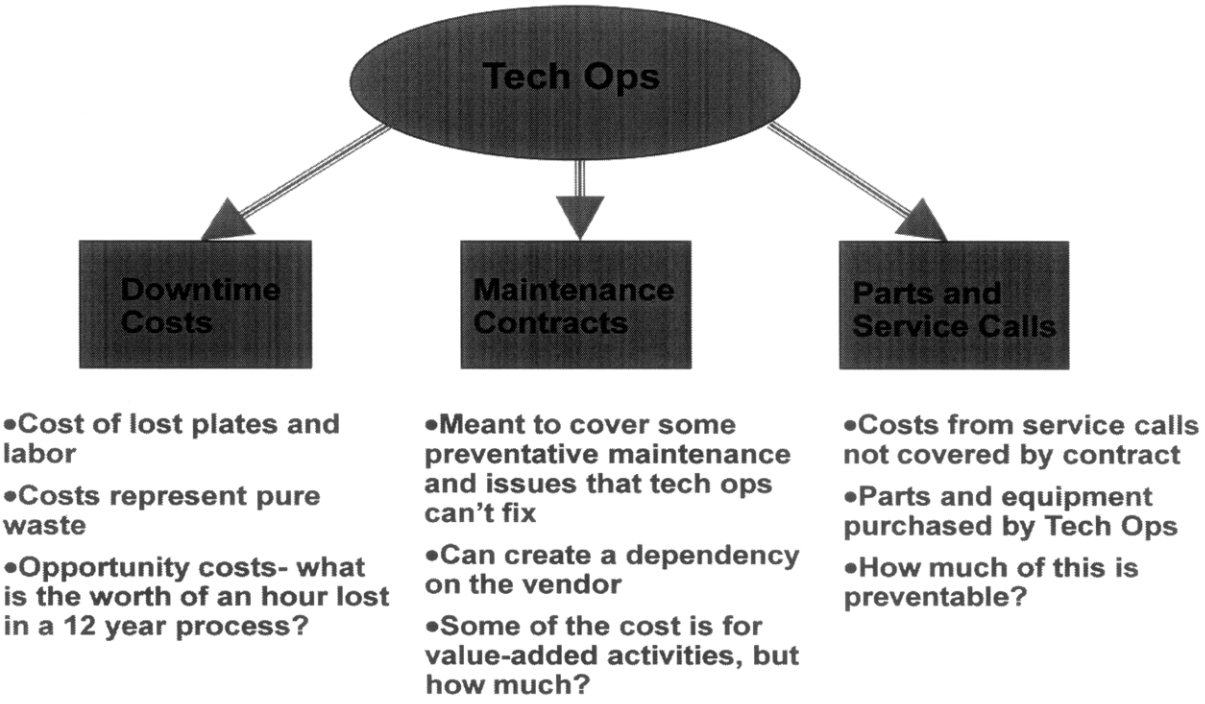

Figure 11. Cost Areas for Maintenance

2.3.1 Downtime Costs

Of all the costs associated with maintenance, the costs due to downtime are the most onerous, as they represent pure waste and even lost opportunity. These costs consist of the lost time and material due to a machine breaking down. When an HTS or P-5 screen goes down, materials can be ruined because the plates often contain time sensitive chemicals. That is to say, some of the reagents used are unstable and will be ineffective after a certain period of time. For some reagents, this instability means that downtime lasting more than 15 minutes can cause plates to have to be thrown away. For others, it is a matter of hours. If the downtime is sufficiently long, the cost of the reagent, the plate itself, and all time involved in preparing it have been completely wasted. In some cases, the screen has to be put on hold for an extra day while the lost plates are being re-plated. This time isn't sufficient enough for a different screener to use the equipment in the meantime, so even if the HTS system was fixed in a timely manner, a day may still be lost. There is also the matter of the time of the engineer to come and troubleshoot the issue. Granted, this is time already paid for, but it could be used for more value-added activities.

These downtime costs do not include the parts required to fix the system or any service calls to the vendor to come in and fix the issue. Those costs are included in another category. Theoretically, this category should also include the opportunity costs of the downtime. As mentioned, drug discovery is essentially a race to patent drugs. Any time lost could mean losing this race to a competitor. However, trying to quantify these costs is a nebulous process at best. Getting a drug to market is a process that takes longer than a decade from start to finish. In that time, how do you put a price tag to minutes lost, or even hours? It has been suggested to take the probability that a screen produces a marketable drug, take the revenue that drug would produce per day, and calculate opportunity cost as the downtime in days multiplied by the revenue lost per day times the probability of a profitable screen. However, the revenue generated from drugs can vary greatly, with some drugs bringing in more than $1B in revenue per year. Also, to date, no drug candidate passing through an HTS system has produced a marketable drug. To be fair, the technology isn't much more than ten years old, so there are HTS-processed drugs in the drug pipeline which should be coming out soon. However, this method of calculating opportunity costs wouldn't produce much confidence in the number, and using it to justify any decisions would be suspect at best. For these reasons, any attempt to quantify opportunity costs has been left out of this study.

2.3.2 Maintenance contracts

Maintenance contracts represent the largest portion of the total maintenance expenditure on equipment for which TechOps is responsible as can be seen in Figure 12. For this reason, there is significant interest in reducing this amount. In fact, NIBR spends more on these contracts than on parts, service calls, and lost plates combined. The interesting thing about NIBR's situation is that they have an in-house team to handle maintenance and repairs; maintenance contracts serve more as insurance than regular service. In the year previous to this study, TechOps suggested getting rid of about $200K worth of contracts. Looking at the data over the past year, they only spent about a tenth of the would-be contract price maintaining that same equipment. This would imply that those maintenance contracts weren't a "good deal" and that getting rid of them was a wise decision. That may be the case, but simply spending less in a given year doesn't always make the best test for these contracts. Few would argue that having health insurance was a poor choice because they didn't get sick that year or that buying home insurance was a waste because their house didn't burn down. There is certainly room for improvement in the way contract purchase decisions are made, but there

are other costs associated with lowering maintenance expenditures. This is part of the reason this study's title is about managing, rather than simply lowering, maintenance costs.

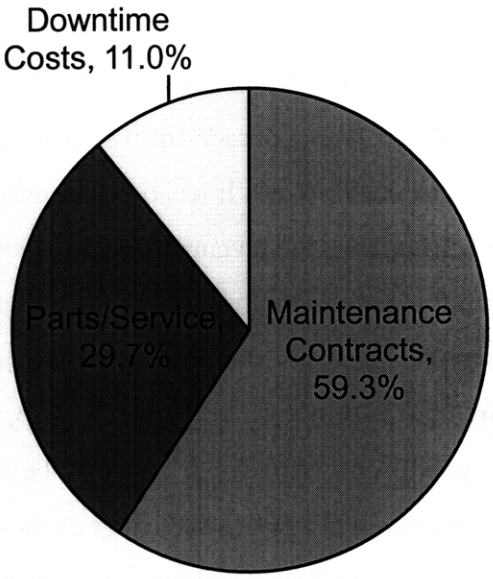

Figure 12. Maintenance Cost Breakdown for NIBR in 2007 (not including in-house labor costs)

2.3.3 Parts and service calls

The final category under consideration considers such things as parts, spares, and service calls not under contract. This category is very much affiliated with how TechOps operates. At the beginning of this study, there was virtually no inventory system. Occasionally, TechOps would order parts that they already had in stock, simply because they couldn't find them. There was also an excess of spares for some systems, while other systems had none. This state of affairs was a casualty of the TechOps tool room. This tool room housed the parts, spares, and tools used by all engineers to service all equipment. In a firefighting system, there isn't much time to spend in finding the best place to store hand tools or small parts. There also isn't much time to look for them, so ordering more is an easy way to handle the problem.

In addition to money spent on parts is the money spent on service calls to the vendors. On occasion, there are problems with equipment that are simply beyond the capability of TechOps to diagnose or fix. This is perfectly understandable, as some systems require special tools that are not

cost effective to keep in house, or they require specialized training that no one in the group has. However, being able to handle more and more of these types of calls in-house not only saves money, it indicates an increase of learning and capability within the group. This not only helps NIBR as a whole, it increases the professional growth and marketability for the engineers, which all will agree is a positive outcome.

2.4 Opportunity Identification

In performing this study it was apparent that there were a number of opportunities for learning and improvement. The original study scope included three things: improving uptime of the automated equipment, analyzing the usefulness of maintenance contracts, and applying lean concepts to the labs. At the outset of the study, it was apparent that downtime wasn't well understood in this context. Therefore, there was great opportunity to look at the process flow and really see where the biggest gains could be made.

2.4.1 Metrics

Related to the issue of downtime are the metrics used to measure performance. One metric TechOps has used is "mean time between failure".. However, it wasn't generally understood as to what that metric meant or how it was measured. Add to that issue the fact that there isn't a reliable data gathering system keeping track of who uses what equipment and when, and there is little confidence in the numbers reported at the end of the year anyway. Research and development was once considered to be an unstructured process that was impossible to manage or control, but opinions have changed as R+D has become a key strategic issue that needs to aligned with overall business strategy. (5) In order to improve this alignment, some sort of performance measurement system is required, both for the drug discovery process and its maintenance.

2.4.2 Continuous Improvement

To measure the performance of the engineers themselves, the evaluation system is somewhat subjective. It is difficult to tell at the end of the day whether or not an engineer has done a good job. This is partially due to the firefighting atmosphere. If an engineer's sole function is to get the equipment back up and running, but there is no standard for how that is supposed to happen, it is

very difficult to gauge performance. Also, if engineers have no time to do anything other than quick fixes, they will never be able to improve performance or learn the root cause of their problems.

Many components fail in a very predictable manner. (2) For example, one common issue with benchtop equipment is the incorrect dispensing of liquid. A screener will specify a certain amount, say 5 micro-liters, and the machine will dispense some other amount (this is noticed when the screener performs a quality check, or QC). The engineer will respond to the call by changing out the valve that dispenses the liquid, perhaps trying to flush it out using the system once or twice to see if performance can be restored. Sometimes, half a dozen valves will be replaced at a time. At around $250 a valve, that can add up. However, the money spent on maintenance isn't given much thought, especially when compared to the potential of drug revenue. That may not be a bad stance to take, and it is a reason for "managing" maintenance costs instead of simply "lowering" them. However, it was noticed that these valves almost always under-dispense as opposed to over-dispensing. This implies that the valve might be clogged in some way. If an engineer could take the time to find out why the valves get clogged, what could prevent it, or even if the valves could be refurbished economically, it would not only save money, but it could save both the screener and the engineer valuable time in the long run. Predictable failures based on use and those that are common due to lack of use should be prevented as part of an annual maintenance plan. (4) Keeping track of these trends requires more effort, but the alternative, firefighting, ends up costing more time than it saves.

2.4.3 Maintenance Contracts

Another major area of opportunity lies in the evaluation of service contracts. To provide some insurance against equipment failures that TechOps can't fix, NIBR buys yearly maintenance and repair contracts with the original equipment vendors. Each department within NIBR handles these contracts for their own equipment, even though different departments occasionally have identical equipment. Thus, there may be potential for more "group rates" when it comes to contract prices. However, there doesn't seem to be much potential to shop around, as the equipment is so specialized that the original vendors are the only ones who provide service contracts. Perhaps the biggest opportunity, though, lies in the question of whether or not a given contract is even necessary. There is potential that NIBR could efficiently cut contracts that would save them over one hundred thousand dollars per year.

2.5 Summary

There is room for improvement in automation performance and maintenance costs within pharmaceutical research and development. Downtime creates waste through lost time and materials in addition to less quantifiable opportunity costs. Parts and service calls are used for problems that perhaps could have been avoided through preventative maintenance or different operating procedures. Finally, it's possible that maintenance contracts aren't providing value that is commensurate with their cost, causing NIBR to overpay for services rendered. It is not clear from the surface, though, how these problems are interrelated, or even what the root causes are. It is easy to point fingers at substandard equipment, glitchy software, insufficient maintenance, or inexperienced operators, but there is no methodology in place for determining performance or even defining what it should be. Without getting to the root causes of downtime or setting performance standards, the group can only guess at how to improve. In Chapter 3, we will discuss different tools for measuring the performance of equipment, engineers, and contracts and how some of them were implemented during this study.

3 Methodology and Analysis

The methodology behind this study consisted of three parallel efforts: putting in a system for collecting appropriate metrics, using continuous improvement projects to change the operational culture, and developing an objective method for analyzing maintenance contracts.

3.1 Data and Metrics

One of the most crucial components of establishing better maintenance practices is to have appropriate data against which to judge performance. These data can and should be collected to gauge the reliability of the equipment, but also should include some information about the process of maintenance itself. Another reason for having this data is that it helps overcome the firefighting culture. If there is no measure or standard to tell the group how they are performing, how can they even tell if they've improved? Likewise, if management doesn't have objective criteria for showing improvement, how can they convince the engineers that they take maintenance improvement seriously? A lack of reliable data, or a lack of the use of the data available, not only keeps the group in the dark when it comes to performance, but it indicates a culture that is content to maintain business as usual.

3.1.1 Appropriate Metrics

To collect these data and use them appropriately, it is important to know exactly what data are needed. At the beginning of this study, the TechOps group was presenting data centered on mean-time-between-failure (MTBF) for the larger automated systems. While MTBF can be a useful data point in some instances, that wasn't the case in this environment. Part of the problem with this was that these data were very unreliable. No one was methodically collecting information as to the usage of the systems, and not all equipment failures were recorded. NIBR uses a custom created maintenance log, called SharePoint, which allows the screener to input a work ticket into the central database when he or she has a problem. TechOps will respond to these issues as they show up in SharePoint. However, any issue that can be fixed by a screener is likely to not get entered into SharePoint, and these issues can be just as relevant, if not more so, to equipment performance. The other major problem with MTBF is that it isn't clear how the use, of lack thereof, of the equipment

plays a role in the number. For example, during this study, one of the HTS systems wasn't used for over a month. During that month, there were no recorded failures, so does that mean the equipment was running smoothly during that time? According to the previous metric system, that is a conclusion that could be drawn. Thus, the lack of use of the system was indicating that it was running properly when, in fact, the lack of use tends to have a detrimental effect on performance evidenced by seals drying out or residual chemicals corroding or clogging parts of the equipment.

To address this issue, it was recommended that TechOps use the following metrics on a per equipment basis: hours spent on scheduled maintenance, hours spent on unscheduled maintenance, plates lost, number of service calls, cost of service calls, and cost of parts replaced. Unfortunately, with the exception of the number of service calls, none of this information was available in any reliable format at the beginning of this study. The purpose of these metrics is to determine the amount of effort spent on any one piece of equipment. It does not address why a particular system went down, but it will allow TechOps to determine where they need to focus more attention and what their maintenance trends are. These metrics will also provide useful inputs when evaluating maintenance contracts. Additional metrics related to the actual usage would also be beneficial, but the collection of such metrics proved to be a lot more difficult. The next section will discuss data collection.

3.1.2 Data Collection

Another important aspect of successfully developing appropriate metrics is knowing how to collect them. In some work environments, a simple notebook can be used to jot down important information about equipment breakdowns and maintenance delays. In other areas, a spreadsheet or another tailored piece of software can be used. However, these methods require that the user be present for these failures and their resolutions, which defeats one of the purposes for having automation to begin with. Using the screener to record key data was attempted in this study, but not only was it prone to user errors and incomplete information, but it was met with resistance. This resistance came mostly in the form of indifference, which is to be expected given the culture that such things are low on the list of priorities for the day's work. Many of the larger or more complex equipment, including all of the automated systems, have their own errors logs that are automatically generated whenever the system shuts down unexpectedly. These systems overcome

the issue of having a person record every problem, but they offer little description of what the problem was. In fact, these logs sometimes can mislead the engineer as to what the problem really is. They also generate a mountain a data that someone has to sift through and monitor to collect the most useful information, something that hadn't been done until the time of this study.

Whether the user or engineer collected the data or whether the software was modified to yield more informative data didn't change the fact that some level of personnel involvement with data collection was necessary. To encourage ownership on the part of the TechOps team, a new system was implemented to collect data based on their own efforts. Instead of trying to track the status of the equipment at all times of the day, this system only tracks what was done to the equipment by the engineers. The system consists of a weekly equipment log that tracks hours of unscheduled and scheduled maintenance for each piece of equipment. The engineers enter in this information according to what they did during the workday. This system is not a tool for keeping tabs on how the engineers use their time, like some management systems. Rather, it is a tool for keeping tabs on the equipment. Because the engineers do other things that aren't directly related to a piece of equipment, it is expected that the log, known as the weekly equipment report, would not add up to a 40 hour work week. The weekly equipment report also keeps record of the other metrics previously mentioned: the number of vendor service calls, the dollar amount spent (on the service calls, parts, and spares), and the number of plates lost. The report also has a scheduling feature that allows the user to set up his scheduled maintenance for the year. An example of one of the weekly equipment reports is found in Appendix B. This system is easy to use, only requiring a few minutes of input per day by the engineer. It also provides value to the engineer in that they can keep a running total on the amount of time and money spent on each machine, so that they can know where their efforts should be placed. Chapter 4 discusses the results of implementing this tool.

3.2 The Spirit of Lean

As previously mentioned, the TechOps group found themselves in a firefighting atmosphere at the beginning of this study. In many ways, the engineers worked for the screeners, responding to their maintenance requests. As can be imagined, a screener can feel that his or her problem is a top priority for the engineer. Not only does the engineer feel some pressure from the screener, but management also wants the group to handle problems as quickly as possible. This is understandable

in the sense that valuable materials can be lost if the system is down too long and also the overall perception that the company's bottom line is more directly tied to the success of the screen than the efficiency of the engineer. However, this has the effect of preventing engineers from taking the time to get to the root cause of downtime. This not only wastes money in terms of maintenance, but it denies the engineer the opportunity to really learn how the equipment operates to the point that he develops a sense of ownership for it.

3.2.1 The NASCAR Analogy

To try and remedy the situation, lean principles were presented to the TechOps group to try and foster a culture of continuous improvement. One of the methods used to demonstrate lean in action was to present to the group the example of the NASCAR pit crew. It was felt by the author that this example would relate well to the demographic of the TechOps team as well as be applicable in the sense that the pit crew is very much like a maintenance team. These pit crews have taken a standard pit stop, which includes changing four tires, adding 22 gallons of fuel, wiping down windshields and radiators, and making chassis adjustments from a time of about 4 minutes in the 1960's to about 12 seconds today. They've done that by appreciating that any improvement, however small, is moving them in the right direction. It is continuous improvement. However, using this example overlooks the importance of incentive. In the NASCAR example, every second lost in the pits means a quarter mile of position lost on the track. A quarter mile on the track can mean the difference between first place and tenth place. That difference can mean more than $100K in prize money, some of which is shared by the pit crew. Thus, they are very much invested in getting better. However, in the case of pharmaceuticals, what is the value of five minutes in a 12-year process? What is the value of an hour? As a maintenance engineer for pharma, lean is a much tougher buy.

3.2.2 Tailoring Lean Principles

A slightly different approach was taken that proved much more successful. In general, lean is something best applied enterprise wide and uses many standard tools such as value stream mapping, Kaizen events, and andon cords. (6) In this study, trying to apply lean enterprise-wide was not only beyond the scope, but lean was perhaps an even tougher sell with the scientific research community. More important than applying specific tools to a situation is to change the culture within that

situation. This is easier said than done, but it is a necessary step if lean tools are going to stick. In order to encourage continuous improvement and develop the "spirit" of lean, TechOps was tasked with going after those issues that were most vexing to their group. For management to identify the problems that TechOps should solve isn't nearly as effective as TechOps choosing their own projects. This provides the group with motivation to do more than get equipment back up and running; it motivates them to improve the work environment, *their* work environment. While the benefits may not be easily quantifiable or felt by many outside of TechOps, they bring about an excitement to improve that is a necessary precursor to lean.

A major theme of applying lean principles is getting to the root cause of the problem. Getting to the root cause is not an easy process, and it takes time and patience. It has been said that causes of problems can be divided into three categories: physical causes, human causes, and latent or organizational causes. Physical causes are such things as faulty valves or leaking fixtures. Human causes may include things such as improperly installing a valve or failing to replace a fixture as appropriate. The organization causes may be that there is no system in place to train the employees on how to install valves or when to inspect the fixtures. It is this last type of cause that TechOps is trying to focus on, as solutions to organizational causes tend to be the most sustainable. (7) The data collection effort is an example of addressing organizational causes. Parts do fail, and the users do make mistakes, but it is likely that putting a system in place that will allow TechOps to see the trends in equipment downtime will be more helpful in properly addressing those failures than trying to address each one as they happen. However, as is stated in Chapter 4, in order to see the results of these efforts they have to be in effect for a longer period of time than was available in this study.

3.3 Maintenance Contract Analysis

The question of when to purchase service contracts can be a challenging one, even more challenging when there is already a maintenance team on site. Ideally, the TechOps team would be able to handle any repair on equipment under their jurisdiction, and there would be no need for these service contracts. That may never be the case, but reducing the dependency on these contracts should be a goal for the group. It certainly doesn't mean that all service contracts are a poor investment, even with an in-house maintenance team. They do provide a means of insurance on bigger problems, and they can also provide cost-effective expertise to the TechOps team that will

enhance their capabilities. An objective analysis is needed to better determine the value of these contracts.

3.3.1 Common Contract Terms

The contract themselves vary as to what kind of coverage they provide, but most have some similar clauses. Most contracts include one to three preventative maintenance visits, where the vendor comes in on a set schedule to perform a list of tasks such as lubrication, alignment, inspection, quality checks, etc. Some contracts will split out the cost for software-only support, which can be a valuable option. A few of the companies that provide these contracts have their own engineers who work within a reasonable distance to NIBR. Many contracts make a provision for how quickly these vendor engineers will respond to a service call, but faster response times mean more expensive contracts. Even so, the fastest response times still only guarantee a less-than-24-hour wait. Likewise, most contracts provide for responding during regular working hours, with overnight service also being more expensive. In some cases, NIBR has to wait for multiple days and a vendor engineer has to fly in from overseas. To keep their costs down, most vendors will try and handle as many issues over the phone as they can, giving instructions to the TechOps engineer. If the problem looks like it is software-related, the vendor may have the power to remotely access the piece of equipment and troubleshoot from afar.

3.3.2 Estimating Contract Value

Trying to quantify the value of these contracts can be a risky proposition, because it depends on unknowns and probabilities. Standard wisdom would indicate that a simple comparison of what the contract costs versus the expected cost of maintaining the equipment without the contract should provide a good measure of the value of that contract. There are a few problems with this logic. The first, and perhaps most obvious problem, is that one can never know with certainty what will be spent on a given piece of equipment in the upcoming year. These contracts tend to be priced at a yearly rate of about 5-20% of what it would cost to purchase the system anew. A catastrophic failure is always possible, regardless of what its probability is. Another problem with this method is that it ignores the value of the service beyond the simple ticket price. Because of their familiarity with the equipment, vendor engineers have a higher probability of being able to correctly diagnose and repair the equipment. Some equipment requires special tools or parts, not all of which TechOps

carries in-stock. Because the vendor is focused on one piece of equipment only, they are more likely to have the parts they need. Thus, service contracts may also provide a measure of quality and time-savings not explicitly represented in a contract price. Lastly, these contracts provide other intangibles such as peace-of-mind that is difficult to translate into a contract line item.

3.3.2.1 Parts and Labor vs. Contract Cost

It should be mentioned here that if TechOps cannot fix a problem and they have no service contract with the vendor, that does not mean they have no way of using the vendor's services. NIBR always has the option of paying the vendor not under contract to fix an issue on a time-and-parts basis. Of course, NIBR is then at the mercy of the vendor as to what the fix will cost. Also, vendors tend to give priority to their clients that have service contracts, meaning that the response time could be lengthened for those purchasing service on a per-case basis. So, how can a pharmaceutical evaluate its insurance contracts? Certainly, the above consideration should be one data point. If an organization consistently spends a lot more on contracts than they receive in actual service, it may be a telling sign to make a change. There are other data points, however.

3.3.2.2 Indispensability

One of the most important pieces of information, and one that makes no reference to contract service level or cost, is the indispensability of the equipment. The indispensability is a measure of the impact of that equipment's downtime. Pieces of equipment with a high level of indispensability include those that are on the drug's critical path, in which any downtime is directly translated into a delay in that drug's progress. It also includes the equipment that comprises the bottleneck of the system. If the equipment can greatly increase a screener's productivity, that could also be considered indispensable. Things that decrease indispensability include redundant capacity and lack of use.

3.3.2.3 Adjusted Replacement Cost

Another data point that may prove useful is the measure of what the in-house team, in this study it's TechOps, is capable of fixing or comfortable with not "insuring". Most contracts will have a hardware price and a software price. The hardware price covers everything physical on the system that the vendor produced. This includes high precision dispensers, sensors, and robotic arms. However, it also includes the desktop computer, the custom table, the plastic guarding, and other

simple or non-moving parts. The point is that a lot of these parts are very unlikely to ever break, and if they did, TechOps would have no problem fixing or replacing them. However, these parts are still paid for under the contract. The table may have been expensive to begin with, but the probability that it will break in such a way that the vendor needs to fix it is extremely low and not worth insuring against. The methodology here is to go through each system on a line-by-line basis with the maintenance team and get their opinion on what should really be covered. The maintenance team is more familiar with the system than anyone in the company, and they can point out what they can fix, what never breaks down, and what isn't even used anymore. Taking the original quote for the system brand new, and paring it down by crossing off those line items that don't need to be insured, one can then get a measure of what the contract costs versus the true replacement cost of the system. In the U.S., service contracts average 10% of the purchase price per year, so TechOps has a value against which to benchmark. (7)

3.3.2.4 Customization

The next data point is the equipment's level of customization. There are actually two dimensions to the term "customization" in this study. The first involves the physical layout of the equipment itself. Some equipment is stand-alone, very standard equipment that a vendor will sell to multiple pharmaceutical companies. These systems are tried-and-true with fewer problems arising that are unfamiliar to the user or maintenance engineer. Some systems are very unique to one or two companies, however. There is still a lot that is unknown about their performance, even by the vendor itself. To make matters worse, some of these fully automated systems involve pieces that are produced by different manufacturers. One vendor put the system together and integrated it, but the contract will still only cover the equipment produced by that vendor. To fully insure the system, separate contracts will be required that cover all manufacturers. The fact that these machines that have been built by separate companies now have to "talk" to each other and work together greatly increases the probability of a shut-down. These unique units are going to require more support than production models. (8) The second dimension is the level to which that equipment can customize its work. As previously mentioned, some equipment is asked to perform a different task every time it is used, while others perform one function and one function only. The latter will be much easier to maintain, both because they tend to have a more tried-and-true design as the vendor produces it

in larger quantities and because engineers are more likely to be familiar with its problems. Consequently, they are also less likely to require a contract.

3.3.2.5 System Age

The last data point used in the evaluation is the age of the system. Most contracts will cover the first year of the equipment as a warranty. After that year, it is up to the client to purchase extended service on a one- or multi-year contract. Hopefully, most major bugs are worked out within that first year, but that isn't always the case. Another important consideration here is how the age correlates in an increase in the engineers' ability to fix the system. Thus, an old system that was purchased brand new and has a maintenance team that has been using it for its lifetime may not require a service contract, but one bought used or with a maintenance team with high turnover might make a contract a wise purchase.

3.3.2.6 Using the Contract Evaluation Tool

The purpose of putting these values together (maintenance costs, indispensability, adjusted replacement cost, customization, and system age) is to have more objective criteria against which to judge these contracts. Some of these values, such as indispensability and customization, are slightly subjective, but they can and should be benchmarked and should stabilize with time. What these values are not, is a fool-proof formula for deciding which contracts to buy. After determining these values for each piece of equipment under consideration, TechOps can then benchmark the contract against one for which they feel they are getting appropriate value. This process will take time as the group decides an appropriate scale for each characteristic, but in the long run it should provide for a more educated decision.

To quantify the effects of the aforementioned considerations, a contract evaluation tool was created that can use data from the metrics developed to score each contract. This tool has six separate modules (parts and labor costs, indispensability, system age, level of customization, adjusted replacement costs, and the weighted average). Each module provides an index for the equipment under consideration. The higher the value of the index, the more value the contract provides to NIBR. The parts and labor module for a fictitious system is shown in Table 1.

Table 1. Parts/labor module of contract evaluator

Parts/labor vs. contract cost		
total value, covered parts replaced last year	$	12,000.00
service calls last year		1
contract cost	$	65,000.00
number of PM's in contract		1
contract value	$	19,500.00
Index value		0.300

This module provides the typical analysis of a maintenance contract. The cost of the contract is compared with the total value received in services over the previous year if the company had the contract that year, or if they didn't have the contract, the amount that could have been saved. In this example, NIBR or the vendor replaced $12,000 worth of parts that were or would have been covered under contract. The number of service calls provides a measure of the labor being provided. For this tool, it amounts to $5,000 per service call. The number of preventative maintenance (PM's) visits is usually stipulated in the contract. For this analysis, we have assumed $2,500 per PM. The index value is the ratio of value received over the previous year to the cost of the contract.

The second module is indispensability, shown in Table 2. The metrics in this module were chosen to make this index less subjective. Each piece of equipment in the lab represents a certain portion of the total capacity in the lab for the function that it performs. This is shown in the first line. Capacity utilization will give a measure of how much the equipment is used, with the idea being that the equipment rarely used is less indispensable. The "ratio of project delay to equipment downtime" is a measure of the impact of downtime on the project's schedule. In this example, for every hour the equipment is down, the project is delayed 0.05 hours. In other words, it has little impact on the schedule. The "percentage of screener time savings over the next best alternative" measures how much of the screener's time is saved using this piece of equipment over their next best alternative, be it performing the operation by hand or using a different piece of equipment. In this case, the screener could save 60% of their time using this machine over their next best choice.

Table 2. Indispensability module of contract evaluator

Indispensability	
percentage, system capacity to total capacity	10%
capacity utilization	15%
ratio of project delay to equipment downtime	0.05
percentage, screener time savings over next best alternative	0.6
Index value	0.232

Table 3 shows the module for system age. This module is intended to capture the effects of age and experience with the equipment on the equipment's downtime. The age of the system at its current location is the length of time NIBR has actually owned the equipment. This is used to differentiate equipment that has been purchased used. The "years of engineer experience" entry captures how many years the most experienced engineer has with that particular piece of equipment, not one just like it. This will give a measure of the capability of the group to handle downtime issues for that machine, and will also reflect some of the effects of engineer turnover on maintenance performance. This module uses an average of the ratios of these values to create the index. The ratio of absolute age vs. expected equipment lifetime trends so that older equipment, which are generally more likely to have problems due to wear, are given higher values. We know from the bathtub curve that very young equipment also tends to have more failures than usual. However, just about every piece of equipment is covered under warranty for its first year, which is why the linear ratio was chosen.

Table 3. System age module of contract evaluator

System age	
absolute age of system, years	5
age of system at current location	5
years of engineer experience	2
expected equipment lifetime	10
Index value	0.367

Table 4. Level of customization module of contract evaluator

Level of customization	
degree of programmability	2
programmability value	0.25
scale number of sister units	10,000
scale value	0.4
Index value	0.325

Table 4 is the level of customization module. As previously mentioned, equipment that is constantly being reprogrammed to do new things and equipment that is one-of-a-kind will likely require more attention. This module is designed to give higher values to that equipment which is highly customized. The values for this module are somewhat subjective. The degree of programmability is the degree to which the equipment can be programmed to perform different function. The user inputs a number between 1 and 5, with "1" meaning "this equipment performs one function and one function only" and "5" meaning "this equipment can be programmed to perform a variety of tasks". The module returns a value between 0 and 1 based on a linear scale. The "scale number of sister units" works much the same way, with the user entering an estimate for the number of identical units of this equipment that have been manufactured. For example, if the user feels that there have been about 500 of these units produced, he or she would enter "100" as the scale, and the module will return a value between 0 and 1. The index is simply an average of these values.

Table 5 is the adjusted replacement cost. As previously mentioned, this is a ratio of the cost of the contract vs. the value of the equipment TechOps would like to insure. This accounts for the fact that there are many things covered under contract that do not need to be with a maintenance team in-house. The index is one minus the aforementioned ratio, to be consistent with having a value of 1 representing the highest possible contract value and a value of 0 the lowest.

Table 5. Adjusted replacement cost module of contract evaluator

Adjusted replacement cost		
system cost (new)	$	446,025.00
adjusted replacement cost	$	400,000.00
contract cost	$	65,000.00
Index value		0.838

Table 6 provides a summary and a weighted average of the indices for the fictitious equipment example. These weights can be used to account for the fact that not all of these indices are equally important. Unfortunately, there wasn't enough data collected at the time of this study to determine what the appropriate weights should be. Looking at the evaluator as currently constituted, it would appear as though the adjusted replacement cost will always have a high value, and system age could be consistently low. The user can adjust these weights with time as better data are collected. More importantly though, each piece of equipment is treated the same, and a comparison can be made that is based on more than cost alone.

Table 6. Index totals for contract evaluator

Totals		
		Weight
Parts/labor	0.300	0.2
Indispensability	0.232	0.2
System age	0.367	0.2
Level of customization	0.325	0.2
Adjusted replacement cost	0.838	0.2
Index value	0.412	

Table 7 gives the values for the actual equipment as calculated with this tool. Not all of the equipment under contract is in this table. This table only represents what data were available, and even in this case, the author had to make estimates for some of the values. However, the basic trends are reasonable. In this case, Company H was chosen as the benchmark contract for the group, as it seems to provide what the group feels is good value. As previously mentioned, this tool will not state which contracts should be purchased and which shouldn't. No tool can say for certain whether a contract will "pay off" for certain as there is always the risk of a major failure. But based on these numbers, NIBR may consider not renewing the Company C, F, or G contracts.

Table 7. Contract Evaluation Results

Totals		
	Overall Index	Difference from Benchmark
Company A	0.497	0.114
Company B	0.497	0.114
Company C	0.390	0.221
Company D	0.479	0.132
Company E	0.558	0.053
Company F	0.360	0.251
Company G	0.384	0.227
Company H	0.611	-

As TechOps collects more data, through the weekly equipment report and their interactions with the screeners, they should be able to refine this evaluator. If they choose not to purchase those contracts and they find they weren't necessary, they can save upwards of $50K per year. If they find that they did need them, then they have new information with which to better the evaluator. With time, TechOps may be able to define a clear cut-off point for the indices, below which they would not purchase a contract. This tool is certainly not at that point, but it frames the questions that TechOps should be asking so that they can make the most educated decisions possible about their contracts.

3.4 Summary

Three different efforts have been introduced to NIBR to aid them with the measurement and improvement of performance from a maintenance standpoint. Engineer-collected data consisting of hours spent on maintenance (both scheduled and unscheduled) and money spent on parts and service calls on a per-equipment basis will help not only encourage the engineers take ownership of the equipment, but allow them to more easily diagnose their own performance and that of the equipment. Lean principles were introduced to the group with an emphasis on addressing organizational causes of waste. Improvement projects were chosen by each engineer as a way to reduce waste and generate momentum for continuous improvement, and they also provide an additional measure by which to gauge engineer performance over the course of a year. Finally, an objective method for evaluating maintenance contracts was introduced that considered the

equipments' maintenance costs, indispensability, replacement costs, level of customization, and age. Chapter 4 discusses some of the findings resultant from these efforts where there were sufficient data from which to draw conclusions. Chapter 4 also discusses the use and purchase of automation in general and how that can affect maintenance and operational strategies.

4 Findings and Discussion

In addition to the findings resultant from the three efforts of the study, a number of conclusions were drawn about the use and purchase of the automation itself. Because operational strategies and maintenance strategies are often intermixed, those findings related to the equipment itself have also been included in this study.

4.1 Description of findings

The results of the study indicate that a new data collection system is necessary and that contracts are going to need to be benchmarked against more parameters than just cost. These changes, in addition to changing a culture, take time. The real test of the results will be if the systems put in place during the study are still being used and improved upon years into the future. At that point, NIBR should have a wealth of useful data from which to plan their operational and maintenance strategies. That being said, there are a number of conclusions that can be drawn from the data that were available at the time of the study.

4.1.1 Downtime

The analysis of the equipment generated data shows that certain errors seem to pop up more frequently. For example, over a two-year period, the HTS systems recorded a "named pipe connection could not be opened" error over 200 times. However, when it came to developing a strategy for getting to the root cause of those errors, the TechOps team indicated that the majority of them were "start-up" errors or simple user-generated errors. What this means is that these errors are easily identifiable and they result in practically no downtime. For example, an error might be generated if a user didn't turn on a certain piece of equipment. The user recognizes the mistake quickly, and the remedy is as easy as flipping a switch. Of course, this doesn't mean systems can't be put in place to try and prevent such an error from occurring, but the seconds of downtime generated are probably not enough to put this error high on the list of priorities. Nor does this mean the equipment didn't have significant downtime, but it does mean that the computer generated downtime data holds little value in its current format. The data logs are difficult to collect and sort through, due to their size and complexity. Typical large pharmas generate over 20 terabytes of data

daily, and someone has to sort through it all. (9) The automation data also require the use of DOS commands or other code to get them in a readable format. Even with the data in a format that is easier to read, the error messages are often cryptic and uninformative. An example of two minutes' worth of this data is found in Appendix C and a collection of error messages as presented by the automation itself is found in Appendix D.

4.1.2 Data Collection Methods

From a data collection standpoint, engineer-generated data proves to be more useful. As part of their continuing improvement effort, the team took the downtime log and adapted it into their SharePoint system so that they had one system to use. They found that keeping a log separate from the service requests on SharePoint was a duplication of effort. The SharePoint system still keeps a record of all the service performed, but it now includes both unscheduled and scheduled downtime, parts costs, and service calls for each piece of equipment. This system will give management a more accurate picture at the end of the year as to what was spent and what was done on each piece of equipment. It won't give any MBTF values, but it will indicate to TechOps what kinds of performance issues the equipment had, what kind of effort TechOps has made to maintain that equipment, and whether any adjustments need to be made.

4.1.3 Continuous Improvement Projects

The improvement projects are ongoing and their effects won't be appreciated until sometime in the future. However, the projects themselves show that the most support for continuous improvement is given by those that stand to benefit from the results. The engineers chose projects that would simply their processes or cut out the waste that was most vexing to their efforts. There is certainly residual benefit to the other organizations within NIBR, but the most important result is that the group is looking for ways to improve upon what they do and get past the firefighting method of operations. In addition, the most successful projects were ones where a single individual performs a significant amount of "legwork" to get a system up and running, and then allows the group to improve upon the system in place. This legwork amounts to creating a prototype for the group. Having something physical in place, be it a written operating procedure, a workspace layout, a set software code, etc., sends a message that change is being made but that there is still time to provide input and make the system what it needs to be. For example, one improvement project was to

make-over the TechOps tool room, providing the engineers with more usable space and making it easier to find the tools they needed. One or two individuals championed this effort, taking the team's input and creating a new tool area that has about the same physical volume as the previous area, but significantly more floor space. "Before" and "after" photos of the tool room are shown in Figure 13, Figure 14, and Figure 15. The team has since added an inventory system for the parts by using bins with barcodes, a computer terminal with internet access so that they can order parts directly from the tool room, and additional tools such as a metal mill to increase their ability to perform repairs. Having one or two people make a first attempt, however good or bad, at these improvement projects builds inertia for continuous improvement because it allows the majority of the group to perform the much easier task of improving upon a system as opposed to building it from scratch.

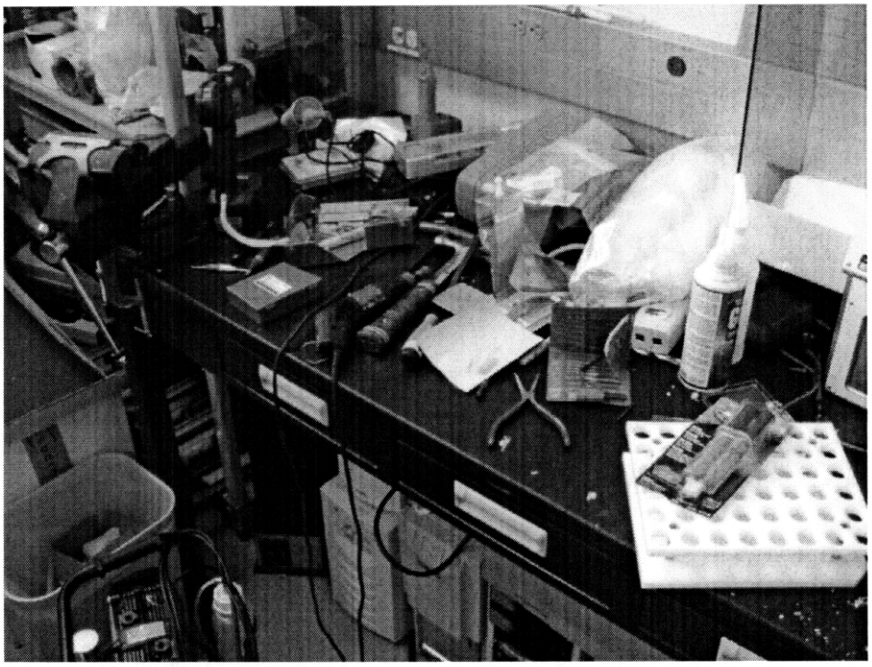

Figure 13. "Before" photo of TechOps workbench

Figure 14. "Before" Photos of TechOps Tool Room

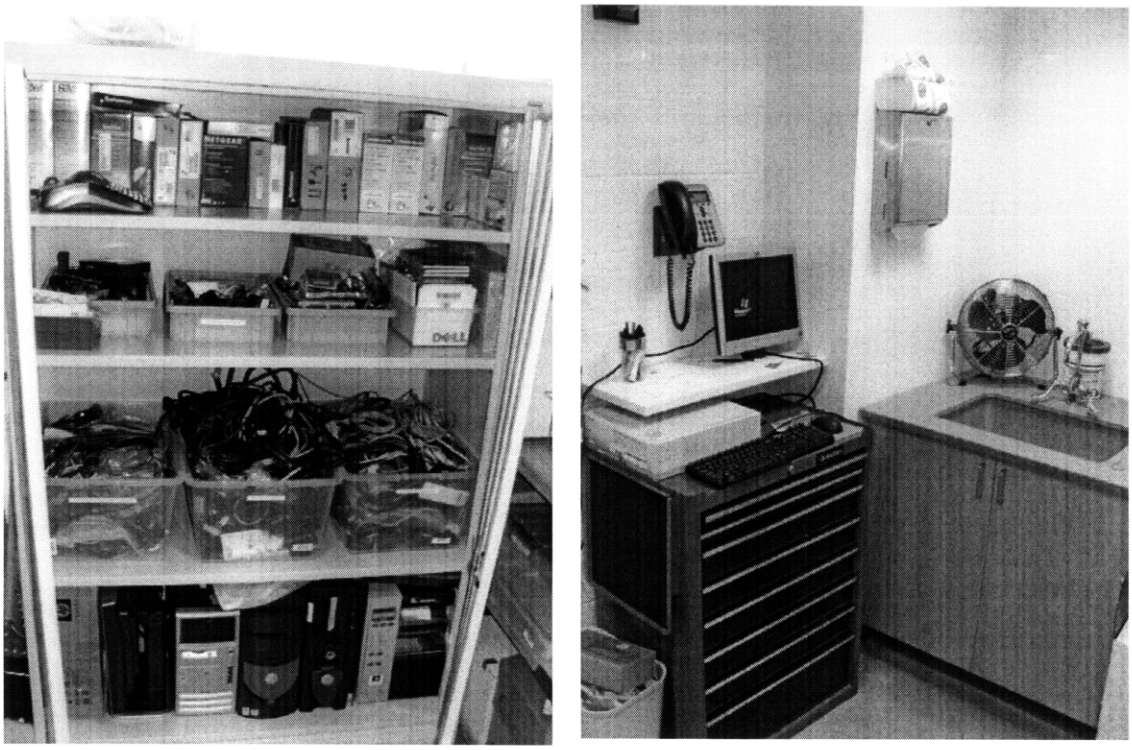

Figure 15. "After" Photos of TechOps Tool Room

4.1.4 Capacity and Utilization

Perhaps the most telling piece of information coming from equipment data comes from a usage perspective. While the automatically generated error data doesn't give much information about root causes of problems, they do give some insight about how much the equipment is actually in use. These recording systems record more than errors; they record every operation that the equipment performs. Walking through the lab, it often appears that certain systems aren't being used, but this can be deceiving as the system may be performing an operation that requires little movement, like incubation. However, from a period between February and November the recorders show all the days when *any* information was recorded, or in other words, all the days when the equipment was used at all. The data in Figure 16, Figure 17, and Figure 18 show that, for the HTS systems during this period, the equipment was used during about 40% of the days of the year. Taking the Saturdays and Sundays out of the data improves the percentage very little, since some of the days the equipment was being used were actually on the weekend. This means that, on average, the HTS systems are run only three days a week. This says nothing about how long the equipment was run on those days, or even if those days were used for actual screens or "dry runs". This would imply that the equipment is underutilized, which is not uncommon in laboratory automation, and that perhaps some effort should be devoted to analyzing the scheduling of the equipment or capacity utilization. (9) Active monitoring of usage data will also help determine whether purchasing particular automation was a good investment. (10)

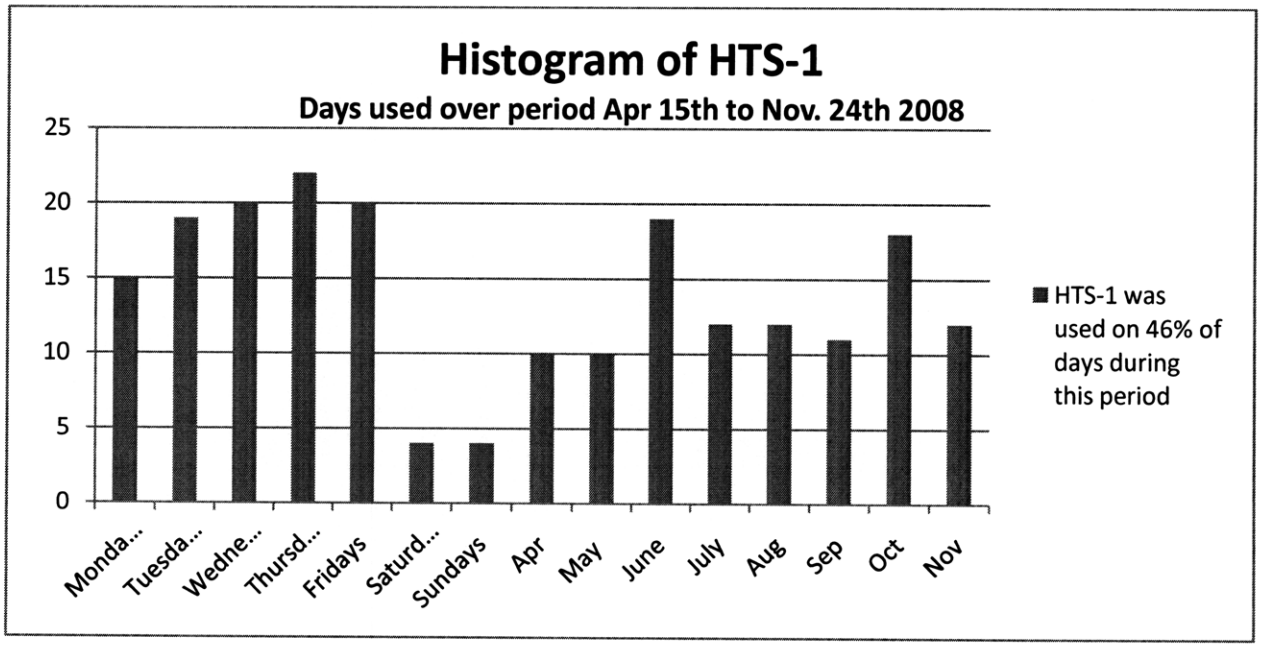

Figure 16. Usage Data for HTS-1

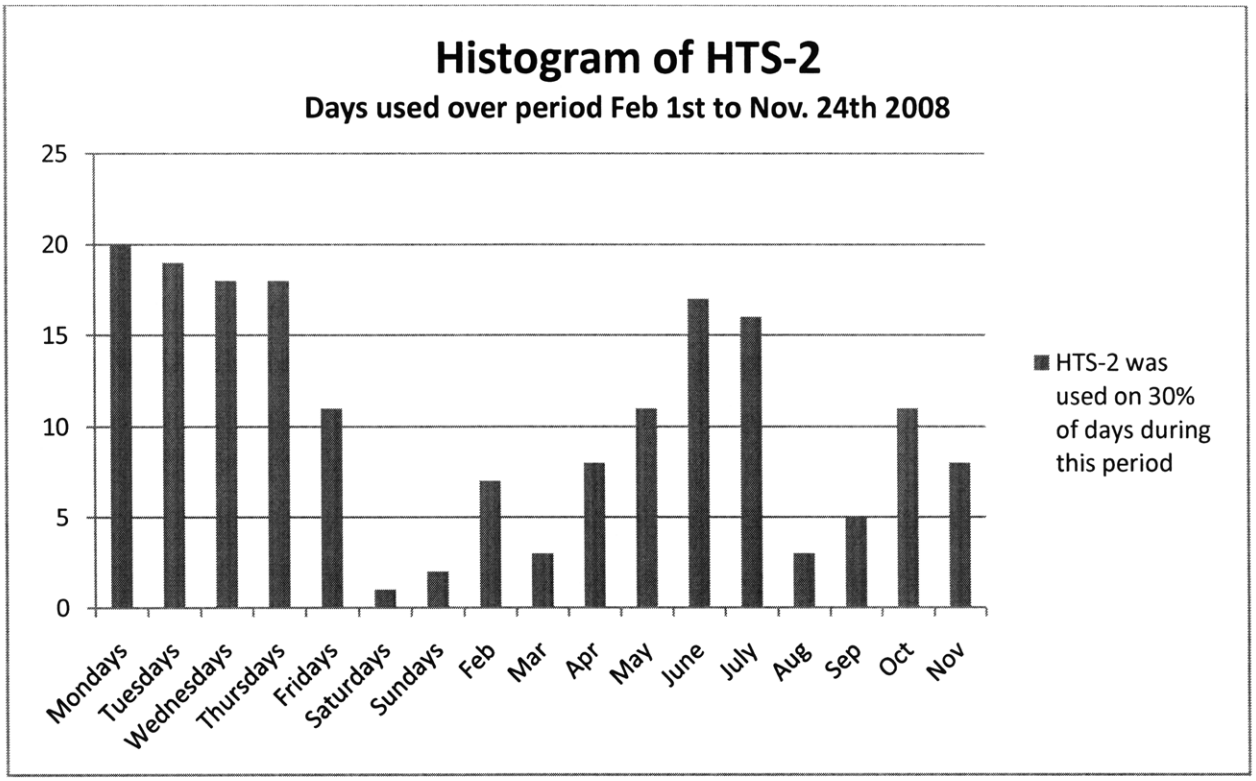

Figure 17. Usage Data for HTS-2

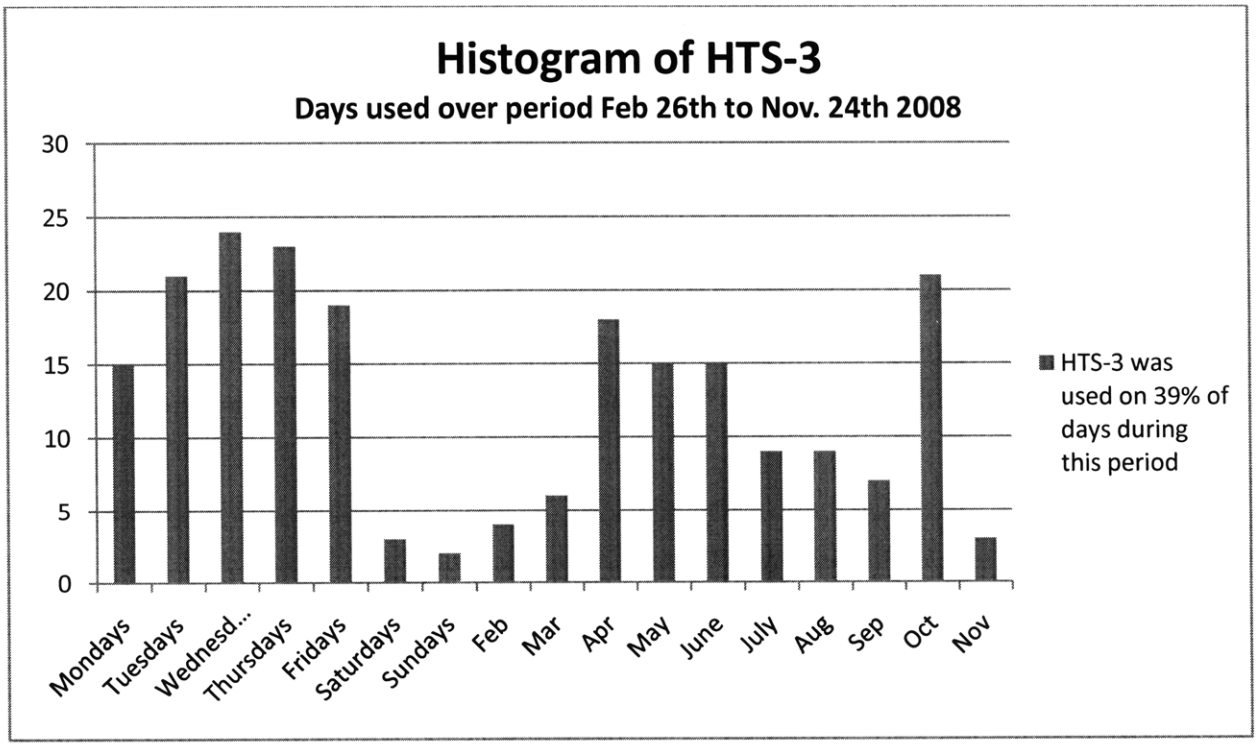

Figure 18. Usage Data for HTS-3

The drug discovery effort has little predictability as there are few standardized processes and the schedule is often undefined. These circumstances create peaks in equipment demand and can only be coped with if a certain amount of overcapacity is available. (11) However, that overcapacity doesn't have to be in the form of complete automation systems. Benchtop units can also provide the flexibility needed by the lab to meet demand, and can do so in a less capitally-intensive manner.

4.1.5 The Use of Automation in Research and Development

As previously mentioned, lowering the costs of maintenance isn't the pharmaceutical company's ultimate goal. The goal is to discover and develop profitable drugs that fulfill an unmet medical need. To that end, there may be a trade-off in which it is better to spend more on maintenance if it translates to more profits downstream. For this reason, one of the most important themes running through this study is that management, the screeners, and the engineers have to know exactly why the automation has been purchased. Interviews and surveys of these groups have shown that there are a number of reasons each individual has for buying the equipment. In a manufacturing environment, the explanation is often that the purchase will yield increased productivity, increased quality control, or lower costs. Pharmaceutical research labs have been purchasing automation for many of the same reasons. (12) Likewise, the screeners also feel that automation is purchased for a variety of reasons (see Q3 of Appendix A). However, realizing these improvements often doesn't occur due to poor implementation or unrealistic expectations. After decades of "growing pains", manufacturing has refined the science of applying automation. One thing that has been learned is automation is not a panacea for all inefficiency in production. With that in mind, let us examine some of the reasons given for using automation in pharmaceutical research and the impact that can have on the operational and maintenance strategies.

4.1.5.1 Increased Productivity

One of the frequent reasons expressed for the purchase of automation is an increase in productivity. There is some ambiguity as to what "productivity" means. In terms of the equipment itself, it may mean that it will allow more screens to be run per year. It is true that automation has the potential to be faster than performing operations by hand. However, unless that automation replaces a bottleneck operation or some operation along the critical path, it won't translate into more screens per year. In fact, it may well be that a screen can be accomplished faster using benchtop equipment.

(13) If more than one screener were used for the same screen, this would most likely be the case. (14) If the group already has more equipment capacity than they use, it is unlikely that buying more equipment will allow more screens to be run. So if productivity is the main goal behind buying automation, the operational strategy would be to utilize as much of the capacity as possible, to try and run as many screens as possible. This, of course, may mean an increase in personnel to prepare the assays, but it also may mean a change in how work is performed. For one thing, running the equipment overnight would take on a much higher priority, and the maintenance strategy would have to be tailored appropriately. Because the risk of downtime is the primary reason for not running overnight, the group should be structured to minimize this risk. There are a number of options for minimizing the risk of downtime while running overnight. These options include allocating more resources to improving equipment performance, buying more capable equipment, using dedicated automation personnel, and having a night staff to handle any problems.

Allocating more resources towards minimizing downtime doesn't necessarily mean spending more money. It may mean spending more time diagnosing equipment errors and finding their root causes. This has the trade-off that screens may be paused for an unspecified period of time while the engineers methodically study the problem. Of course, the idea here is that, as the engineers learn more about the equipment, steps can be taken to prevent failures from happening in the future. If the goal is to just get the equipment back up and running as fast as possible, problems are likely to recur.

There is always the possibility that the equipment on hand simply isn't the best suited for the job. There are usually a few options when it comes to picking out any piece of automated equipment, and not all are created equal. It may be that one system is more robust than another and more likely to run with little intervention. Other systems may be capable of greater capacities or speeds that will result in an increase in the number of screens. In this case, it is important to make sure the equipment is reliable first and fast second. One observation from the study of NIBR is that a less reliable system will see much of its capacity wasted. Downtime not only replaces what could be productive time, but it also has a tendency to dissuade the screener from using that piece of equipment. Some screeners will continue to do some operations by hand if they feel the alternative is unreliable.

If productivity is the prime reason for buying automation, having dedicated operators makes sense. At NIBR in Cambridge, the screeners are the scientists. While the scientists have the most intimate knowledge of the screen being run, in HDG they only use the equipment for a few months out of the year. The result is that the scientist will have to re-familiarize him- or herself with the equipment. Anyone who has used a complicated piece of software knows that trying to do new things with it after not having used it for a long time is not "like riding a bike". Having a core group of personnel who use the equipment year round can eliminate a lot of the user errors that occur at the beginning of a screen. One option would be to use the engineers as the equipment operators. They would receive the assays from the scientists and perform the screen or whatever operation was deemed necessary. This might require hiring more engineers, but it would also allow them to better learn the finer points of the equipment they are responsible for maintaining. Another option would be to hire a separate staff that only ran the equipment. They would become the expert operators and would also most likely cost less on a per-hour basis than using the scientists as screeners.

The biggest concern with running automated systems unattended overnight is that they can shut down completely and no one is there to fix them. NIBR has set up limited monitoring systems so a screener can investigate from home whether his or her own screen is still running. However, if the screen stops, their only recourse is to either go back in to work and try and fix it themselves (or perhaps convince a engineer to come in) or allow the system to sit until morning, in which case expensive materials will surely have to be thrown away as their potency has expired. Sometimes, all that is required to "fix" the problem is simply pushing "Re-try" on the computer, but there is no way of knowing that or doing that from home. The simple prospect of having to get out of bed to save a screen is enough to convince many screeners to run only during the day. Having an overnight staff could remedy this situation. A very small number of screeners and one to two engineers would be sufficient to keep equipment running overnight. Since there are only a few systems for which running overnight makes sense, a small crew should be able to handle most problems. This may mean that screeners who run during the day would have to trust their screen to someone else at night, but it could greatly reduce the time required to complete the screen.

4.1.5.2 Increased Walk-away Time

Another reason given for purchasing automation is that it makes the screener more productive. The less time a screener has to perform manual tasks such as pipetting, filling bottles, and moving plates, the more time he or she has to analyze data or otherwise perform the science for which he or she was hired. This is also known as "walk-away time". Automation can increase the walk-away time for these individuals allowing them to perform more value-added activities that a machine isn't capable of duplicating. In this scenario, it is okay to have some idle equipment (from a capacity standpoint), since that is preferable to having idle employees. (8) This is a perfectly legitimate reason for buying automation, but it is important to keep a few things in mind. First of all, the survey taken of the screeners showed that they still spend an average of 10% to 25% of their day monitoring or otherwise being present at the equipment. More downtime will tend to make that percentage even higher. Thus, automation time doesn't completely replace screener time. Also, maximizing walk-away time may require a change in how the group operates. NIBR tends to give priority to the more complicated screens when two screens are competing for a piece of equipment. However, more complicated screens tend to have more issues that require user attention. Thus, to maximize walk-away time, the less complicated screen should in fact get priority, moving the more complicated screen to the benchtop equipment.

4.1.5.3 Increased Quality

It is possible that a new technology comes out that will increase the overall capability of the group. Perhaps this technology will translate into an increased potential to discover new drugs. More often, though, new technologies simply provide more confidence in the data generated by adding precision to tasks previously done by hand. If this is the reason for buying the equipment, it is important to understand the story leading up to that need. What is the confidence level in the data right now? What are the causes behind having bad data? What are some of the collateral effects of bringing in a new technology? Too often, automation purchase decisions are spurred by a desire to use a new technology as opposed to actual automation needs. (8) A study of the equipment at NIBR indicated that some of the equipment never performed as expected at the time of purchase and some never had concrete data to justify their purchase.

4.1.5.4 Lower Cost

Buying automation to reduce costs is a common tactic, particularly when a firm believes that technology can replace a good portion of their workforce. In the case of NIBR, it isn't likely that the labor force will be reduced through replacement by automation. However, there still may be a case for automation that can lower costs. Machines that can use smaller amounts of materials, can run on less power, or result in a higher yield can also reduce costs. In this case, the procedure should be much the same as when purchasing equipment to increase quality: there needs to be an accurate picture of the current situation. What are the operational costs? How much, exactly, are the expected savings with the new equipment? Likewise, project success criteria are needed before any investment is made. (2) At the time of this study, it didn't appear that current costs or expected savings had been calculated for any of the recent purchases. However, interviews of those involved in purchase decision indicated that lowering costs was considered an added benefit rather than the primary purpose of buying equipment. Regardless, understanding the current situation is a necessary precursor to claiming cost benefits. With those answers in place, it would then be beneficial to examine the potential for lowering costs of the existing equipment by making organizational changes. With those options exhausted, the group can then consider buying new equipment.

4.1.5.5 Talent Retention

It has been said that automation is also a marketing tool and that it increases the quality of life for the screener. Automation can attract the investor that believes that a company willing to invest in technology is more capable of finding profitable drugs. It can also attract the talent that is in high demand for researching these drugs. In that sense, the screener views running the automation as a job perk. The screeners themselves have various reasons for preferring automated equipment, but one of the most popular is that it improves their quality of life. It prevents the screener from having to do a lot of repetitious, monotonous work. It allows them a more comfortable workday while still being able to get their work done. There is a downside to this, however. If the equipment is unreliable, it may have an opposite effect on personnel. The survey taken of screeners shows that, in some cases, they feel that even the smallest amount of downtime can be a major nuisance to them, making them less effective. Thus, simply having automation does not necessarily provide the full benefit.

4.1.5.6 Summary

All of these reasons may be valid ones for purchasing automation. With the proper due diligence of determining the current state, management can make a good case for making a purchase against any of these reasons. It may be the case that there are multiple reasons to buy or use automation. However, believing that automation is purchased for *all* of these reasons not only runs the risk of not meeting expectations, it makes it very difficult to design an operating or maintenance strategy in keeping with the goals of the purchase. A comparison of these reasons and their effect on strategy is summarized in Table 8.

Table 8. Operating and Maintenance Strategies for Automation

Automation Goal	Operating Strategies	Maintenance Strategies
• **Increased Productivity (more screens per year)**	• Consider adding more screeners instead of machines • Run small overnight shift • Reserve Capacity	• Run small overnight shift • Emphasis on preventative maintenance
• **Increased Walk-away Time (scientist productivity)**	• Scientists hand over screening to engineers • Give automation preference to more standard screens	• Engineers operate automation
• **Increased Quality**	• Keep meticulous data on quality • Seek to standardize operating procedure	• Perform routine preventative maintenance • Quality checks
• **Lower Cost**	• Keep meticulous data on cost (operating and maintenance) • Thorough analysis/testing before new automation purchase • Consider balancing higher risk screens (unstable and/or expensive reagents) with lower risk technology (less automated or more reliable equipment)	• Root cause analysis and preventative maintenance • Maintenance contract analysis • Should be involved in automation purchase decisions
• **Talent Retention**	• Determine degree to which talent values operating the equipment • Determine impact downtime has on the morale of the screener	• Provide necessary training for new equipment

4.2 Policy Recommendations

A major theme throughout this study is that both operational and maintenance metrics should be put in place that are easily quantified, provide an honest measure of performance, and are accessible to screeners and engineers alike. It is safe to say that this recommendation holds true for most organizations. Equally applicable recommendations include limiting the purpose of automation purchases to just one or two goals, formalizing the maintenance contract analysis, and placing an emphasis on continuous improvement through projects of the agents' choosing. However, there are a few specific points the author wishes to reiterate that are more germane to NIBR:

1. In the case of two screens needing HTS at the same time, unless there is a correlation that shows that more complex screens require better data accuracy or some other benefit unique to the HTS systems, more complex screens are better left to the benchtop equipment. Giving preference to automation-friendly screens with a large number of samples will give the automation a better chance of running without any failures, improving capacity utilization. (2)

2. The current method of getting the equipment back up and running as quickly as possible seems to improve productivity, walk-away time, etc. by reducing the average time spent in repair, but it costs more in the long run. (15) These costs include the materials that might have been saved or refurbished through careful maintenance, the excess total time spent repairing issues that could have been prevented, and the loss of learning opportunities that are present in the root cause analysis process, not to mention the repeated hassle it creates for screeners. A culture that is quick to buy additional equipment can magnify the loss of learning opportunities, as it is easier for a company in a rich industry to buy excess capacity than learn how to get more out of existing equipment. Considering that the data show that the HTS systems are only used on three or four days out of the week on average, it is recommended that no new capacity be added until the metrics show that it is necessary.

3. In the case of automation purchases for NIBR, favor equipment with increased reliability over increased speed or capacity. Because NIBR often doesn't run automation overnight due to the risk of automation errors, the most reliable equipment will probably become the most productive.

4. NIBR should consider having the engineers run the equipment full time. Making this change will maximize the walk-away time of the scientists, develop a clear sense of ownership on the part of the engineers, and will likely reduce downtime through fewer user errors and an increased familiarity with the workings of the machines. Before this change can be made, NIBR should determine what the fallout would be on the part of the current screeners. In a survey taken of the screeners at NIBR, almost all of those responding felt that automated equipment made them more productive, but only one felt that the automated equipment was reliable. This productivity, as they explained it, was the increased time to do other things like data analysis and feeling less burned out from doing the screens by hand. Even if the automation were completely turned over to the engineers, it may be true that the benefits to the screeners outweigh any disappointment over the change in procedure.

5. It is recommended that NIBR adopt the contract evaluation tool, adjusting the indices according to the experience of the screeners and engineers, and make some conservative contract purchase decisions according to the tool's outputs. The results from these decisions will provide valuable input towards fine-tuning the tool for the following year.

4.3 Summary

In general, the data that were available at the beginning of the study were all automation-generated data. This data proved to be of little value from a root cause analysis or even a performance standpoint, as the data give no indication as to the severity or the cause of the downtime. The data did, however, indicate that the HTS equipment is underutilized, being used an average of three days per week. Data collection methods proved to be more sustainable when tied in to TechOps existing database in SharePoint. TechOps is currently collecting information including hours of unscheduled and scheduled maintenance per piece of equipment, the cost of parts and labor, and the number of service calls. This information is easily summarized so that management can track performance.

However, by the end of this study, the data collection effort had only been in place for little over a month, making it unreasonable to draw many conclusions from the data. By the end of the following year, though, TechOps should have valuable information to help them improve performance. The completed improvement projects, such as the TechOps tool room, were generally well-accepted by the team and, if continued in the future, will help to shift the group away from firefighting. The contract analysis tool gives an objective measure by which to judge contracts. This tool will require some trial-and-error to determine appropriate factor weights and to benchmark appropriately. However, the tool is easily modified and, as it is refined, will help determine at what cost service contracts no longer make sense.

The use and purchase of automation was also discussed, with the main point being that a pharmaceutical company should have a clear picture of exactly what they want the automation to accomplish before purchasing. With one or two major goals in place, the company can then tailor its operational and maintenance strategies to support those goals. This reinforces the need for appropriate metrics, as they will help determine if the automation is accomplishing the purpose for which it was intended. Maintenance and operational strategies were summarized according to the goal of the automation. Because some of these strategies conflict with one another, an automation project that seeks to realize every conceivable benefit will underperform by definition. Chapter 5 summarizes this study.

5 Summary

Within the pharmaceutical industry, automation equipment is tasked to handle precise quantities of millions of compounds, often performing operations in a different fashion every run, and often by a different operator. It is reasonable to expect that an operational system with so little standardization will be prone to a high number of equipment errors. The direct costs of these errors are relatively small given that such a small quantity of materials is at risk at any one time. However, the indirect costs of these errors are much more difficult to quantify, and can range from screeners refusing to run the equipment unsupervised to losing a patent due to the delay in getting the product to market. With these errors occurring so frequently, it is easy to design a maintenance system around getting the equipment operating again as quickly as possible. This leads to a firefighting culture that never gets to the root cause of the automation errors. This system will ultimately be more expensive as problems reoccur and parts are replaced that could have been salvaged.

Maintenance isn't all about minimizing cost, however. When downtime can have an effect on revenues or talent retention, it may be judicious to spend more on maintenance. For this to be the case, it is important to understand that exact purpose for having the automation to begin with. Pharmaceutical companies use automation within their laboratories for a number of reasons. These reasons may all be valid, but it is unreasonable to expect automation to solve all problems. Automation that is purchased for one or two specific purposes will provide more reasonable expectations. Even before that purpose can be determined, the lab needs to have metrics in place that accurately describe equipment and procedural performance. Once these metrics are in place, not only can the lab determine where they are deficient, but they can design an operating and maintenance strategy around achieving that purpose. This case study supports the idea that metrics can be used to manage spending on maintenance contracts, encourage maintenance engineer performance, and avoid potentially unproductive automation purchases. It is recommended that NIBR determine the purpose for its automation through more quantifiable data and seek to maximize the performance of its current assets to that effect.

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APPENDIX-A

Complete screener survey results

Q1

Automation at Novartis		
Which of these systems do you use most often?		
Answer Options	**Response Frequency**	**Response Count**
HTS	55.6%	10
SelecT	11.1%	2
P-5	11.1%	2
SolAr	16.7%	3
I do not use any of these systems	5.6%	1
	answered question	**18**
	skipped question	**0**

Q2

How often do you use automated equipment?		
Answer Options	**Response Frequency**	**Response Count**
Never	0.0%	0
Daily	33.3%	5
Weekly	13.3%	2
Monthly	0.0%	0
A few weeks a year	6.7%	1
A few months a year	46.7%	7
	answered question	**15**
	skipped question	**3**

Q3

In your opinion, what are the benefits of automation?		
Answer Options		**Response Count**
		11
answered question		**11**
skipped question		**7**
Number	**Response Date**	**Response Text**
1	09/17/2008 17:33:00	automated scheduling, walk away time, consistency between runs
2	09/17/2008 18:15:00	more free time and less working intensity
3	09/17/2008 18:18:00	if it behaves, sceening is faster and less tedious
4	09/17/2008 19:10:00	Hands off while work is being done by machine
5	09/17/2008 19:15:00	Reproducability, error reduction, reduced staffing burn-out
6	09/17/2008 21:30:00	efficiency: amplification of effort. consistency and improved quality of data.
7	09/29/2008 18:01:00	increased efficiency, increased accuracy
8	10/08/2008 14:05:00	engineering and science are difficult to mesh
9	10/08/2008 15:25:00	It shortens the time one has to run a screen. This increases productivity and allows more time for data analysis.
10	10/13/2008 19:06:00	each sample is treated the same, can work outside the 8 hour workday
11	10/16/2008 20:29:00	Though not faster than people, the SelecT performs large repetetive tasks instead of people during working hours, and evenings/weekends.

Q4

On average, what is the effect of equipment failure on your daily activities? (only for days you intended to run a piece of equipment)							
Answer Options	No effect- I can easily do my work some other way	Little effect- I can simply reschedule my day and accomplish other important tasks	Some effect- I can do other things, but it definitely makes an impact	Large effect. I have to make major changes to my plans, and I've lost time.	Largest effect. It is a major nuisance and it limits the effectiveness of my day.	Rating Average	Response Count
If equipment is down for 0-4 hrs	1	3	7	1	3	3.13	15
If equipment is down for 4-8 hrs	1	0	3	5	5	3.93	14
If equipment is down for 1-2 days	0	0	1	7	6	4.36	14
If equipment is down for more than 2 days	0	0	1	5	8	4.50	14
					answered question		15
					skipped question		3

Q5

What effect do concerns about machinery reliability play in your decision to run automated equipment overnight?		
Answer Options	Response Frequency	Response Count
No effect	0.0%	0
Little effect	20.0%	3
Some effect	40.0%	6
Great effect	40.0%	6
	answered question	15
	skipped question	3

Q6

Which of the following are true about automated equipment, in your opinion:		
Answer Options	**Response Frequency**	**Response Count**
It's faster, allowing me to move on to a new project sooner	46.7%	7
It improves the quality of my work	53.3%	8
It is convenient	33.3%	5
It makes me more productive	73.3%	11
It is dependable	6.7%	1
I prefer it over more labor-intensive alternatives	60.0%	9
None of the above	0.0%	0
answered question		**15**
skipped question		**3**

Q7

When running automated equipment during the day, how much of the run do you spend monitoring or otherwise present at the equipment?		
Answer Options	**Response Frequency**	**Response Count**
Less than 10%	26.7%	4
10-25%	46.7%	7
25-50%	20.0%	3
Greater than 50%	6.7%	1
answered question		**15**
skipped question		**3**

Q8

Answer each question according to your experience:

Answer Options	Never	Rarely	Sometimes	Usually	Always	Rating Average	Response Count
I contact Tech Ops when the equipment stops unexpectedly	0	1	7	2	5	3.73	15
I clean or perform other maintenance on the equipment when I use it	0	0	1	5	9	4.53	15
I follow a written procedure when using the equipment	0	7	1	3	3	3.14	14
I feel comfortable using the equipment with little assistance	0	1	2	2	10	4.40	15
I feel that equipment problems are handled promptly	0	0	2	10	3	4.07	15
I feel confident that the equipment can run overnight without a problem	0	3	6	5	1	3.27	15
The automated equipment is functioning properly when I am scheduled to start using it	1	0	2	8	4	3.93	15
Any redo plates that I request or process are a result of automated equipment not functioning properly	1	2	2	7	3	3.60	15
I have had to delay moving forward with a project because all equipment I could use (including benchtop equipment) was either in use by someone else or not in service	2	6	5	2	0	2.47	15
						answered question	15
						skipped question	3

Q9

In your opinion, what is the biggest problem you face when using (HTS, SelecT, SolAr, P-5)?		
Answer Options	**Response Count**	
	13	
answered question	**13**	
skipped question	**5**	
Number	**Response Date**	**Response Text**
1	09/17/2008 17:42:00	not able to be notified if error occurs when we are not at work. some problems could be resolved remotely.
2	09/17/2008 18:10:00	Reliaility
3	09/17/2008 18:23:00	liquid handlers like flexdrops on the hts require frequent qcs, clean-up is a bear!
4	09/17/2008 18:26:00	reliability
5	09/17/2008 19:16:00	Getting time on the system when no one is using it.
6	09/17/2008 19:24:00	System design limitations leading to impact on capacity/throughput
7	09/17/2008 21:38:00	specialised knowledge is not widely disseminated.
8	09/29/2008 13:59:00	Often the assay itself governs whether or not the equipment needs to be used over night (ex. cell based assays with long incubations) therefore monitoring issues at night is difficult. My biggest problem is a push from management to continue running even when issues are occurring. There is also a push to run as many days a week as possible even if it means coming in on weekends for people (whether to clean equipment or set up cells) still persists. When speaking to the group as a whole there is a lot of lip service that weekend work isn't necessary. But then when it comes down to planning your screen on a more private level there is a push to run as much as possible even when it involves weekends. Basically, its not the automation that's the problem. Just a need to see that green light all the time.
9	10/08/2008 14:11:00	instrument crashes overnight
10	10/08/2008 15:37:00	If there is a problem after hours, I am reticent about calling Tech Ops for assistance given their personal responsibilities outside of work. One then has to do as much troubleshooting independently as possible, without causing further damage to the system. If the problem is insoluble, then that day's run is lost. It would be beneficial if there was after hours assistance during overnight runs on The HTS systems.
11	10/08/2008 16:27:00	System has a error during the run.
12	10/13/2008 19:12:00	HTS systems - robot errors, flex drop tip clogs, vspin errors
13	10/16/2008 20:50:00	SelecT: The UNEXPECTED component failure that can't be pin pointed by a schematic or log file, and needs a massive tear down to access and reconcile failed component. Will require days and many down stream projects suffer.

Q10

In your opinion, what can be done to improve the reliability of the equipment you work on?		
Answer Options		**Response Count**
		11
answered question		**11**
skipped question		**7**
Number	**Response Date**	**Response Text**
1	09/17/2008 17:42:00	keep as few people using it as possible, including tech ops. a little knowledge is enough to create big problems
2	09/17/2008 18:23:00	regular qcs of all liquid handlers
3	09/17/2008 18:26:00	better maintenance
4	09/17/2008 19:16:00	Update some of the readers on the system and keeping up on some of the QC checks.
5	09/17/2008 19:24:00	Replace worn parts
6	09/17/2008 21:38:00	more people could take a greater concern, overcoming the inertia when things break down / items needed get lost/ upkeep of machine is easier as everyone is doing it routinely .
7	09/29/2008 13:59:00	Things have improved immensely in the last few years regarding equipment reliability. I think people caring for, monitoring QC, and cleaning equipment properly will further improve the situation.
8	10/08/2008 14:11:00	BAT should not be done for every assay that passes through
9	10/08/2008 15:37:00	I have no recommendations as to improving equipment reliability. Given that Tech Ops does routine maintenance, there aren't many other options to increasing reliability of equipment.
10	10/08/2008 16:27:00	Purchase more reliable equipments than the ones we have. Make HTS as simple as possible (equiment combination)
11	10/16/2008 20:50:00	Failed belts, hoses, valves, etc can usually be isolated and reconciled reasonably quickly and I have spares. Factory PM performed yearly. If a controller, fan, cell counter or pipette head fails- It's a one off event- but devastating to the process. A redundant (second) sytem would be helpful, as we are planning more capacity upgrades to the current system- leveraging more down stream projects on a single system. I think using standard plates for all assays if possible is helpful and would eliminate the occasional plate mis-pick problems that seem to crop up. Redundancy (A second system or CompacT selecT).

APPENDIX-B

Example of a weekly equipment report (partial)

Week of:	6/23/2008							
Equipment	Unscheduled Maintenance, hrs	Scheduled Maintenance, hrs	Plates Lost	Number of Service Calls	Parts Replaced? (Y/N)	Dollars Spent	Scheduled Maintenance to be Performed	Comments
TO-BioStack A		1					see vendor manual	
TO-BioStack B		1					see vendor manual	
TO-BioStack C		1					see vendor manual	
TO-CyBiWell 1								
TO-EDC 1								
TO-ELx405 D								
TO-EnVision 1				1	y	0		this was covered under contract
TO-EnVision 2								
TO-EnVision 3								
TO-EnVision 4								
TO-EnVision 6								
TO-Equator 1		2					vendor-recommended	
TO-FlexDrop 12								
TO-FlexDrop 13	0.5				y	250		replaced valve
TO-FlexDrop 14								

APPENDIX-C

Portion of automation-generated master log for a typical run. (Represents about two minutes worth of data)

[2008/06/20 11:56:24] INFO: [] Initializing sample and container status ...
[2008/06/20 11:56:24] INFO: [] Initialized sample and container status ...
[2008/06/20 11:56:24] INFO: [] Starting run.
[2008/06/20 11:56:25] INFO: [] Starting processing of sequence file "C:\Program Files\CRS Robotics\POLARA\Workspaces\Add CMP_moat.sq000"
[2008/06/20 10:56:25] INFO: [I=1(belt)] belt Mover Administration Daemon
[2008/06/20 10:56:25] INFO: [I=1(belt)] MAD Port 27000
[2008/06/20 10:56:25] INFO: [I=1(belt)] MAD Port 27000moverd vmoverd.html revision 65
[2008/06/20 10:56:25] INFO: [I=1(belt)] MAD Port 27000moverd vmoverd.html revision 65Black Box 0, port 0
[2008/06/20 10:56:25] INFO: [I=1(belt)] Simulation mode is disabled
[2008/06/20 11:56:25] INFO: [] Sequence file started.
[2008/06/20 11:56:25] INFO: [] Program /host/_addremove.r is started with pid 29
[2008/06/20 11:56:25] INFO: [] Starting Add Remove Container Program (C:CRShost_addremove.temp.r3)
[2008/06/20 10:56:25] INFO: [I=1(belt)] MAD Server ready
[2008/06/20 10:56:26] INFO: [I=2(FLIPFlexdrop1)] FLIPFlexdrop1 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=4(FLIPlpx1)] FLIPlpx1 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=3(FLIPFlexdrop2)] FLIPFlexdrop2 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=4(FLIPlpx1)] MAD Port 27003
[2008/06/20 10:56:26] INFO: [I=2(FLIPFlexdrop1)] MAD Port 27002
[2008/06/20 10:56:26] INFO: [I=3(FLIPFlexdrop2)] MAD Port 27013
[2008/06/20 10:56:26] INFO: [I=4(FLIPlpx1)] MAD Port 27003moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=2(FLIPFlexdrop1)] MAD Port 27002moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=3(FLIPFlexdrop2)] MAD Port 27013moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=4(FLIPlpx1)] MAD Port 27003moverd vmoverd.html revision 65Black Box 0, port 3
[2008/06/20 10:56:26] INFO: [I=5(FLIPlpx2)] FLIPlpx2 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=3(FLIPFlexdrop2)] MAD Port 27013moverd vmoverd.html revision 65Black Box 1, port 3
[2008/06/20 10:56:26] INFO: [I=2(FLIPFlexdrop1)] MAD Port 27002moverd vmoverd.html revision 65Black Box 0, port 2
[2008/06/20 10:56:26] INFO: [I=8(FLIPlidder)] FLIPlidder Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=4(FLIPlpx1)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=3(FLIPFlexdrop2)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=5(FLIPlpx2)] MAD Port 27011
[2008/06/20 10:56:26] INFO: [I=2(FLIPFlexdrop1)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=5(FLIPlpx2)] MAD Port 27011moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] VALcytomat44 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=7(FLIPstx1)] FLIPstx1 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=5(FLIPlpx2)] MAD Port 27011moverd vmoverd.html revision 65Black Box 1, port 1
[2008/06/20 10:56:26] INFO: [I=8(FLIPlidder)] MAD Port 27023
[2008/06/20 10:56:26] INFO: [I=5(FLIPlpx2)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=8(FLIPlidder)] MAD Port 27023moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] MAD Port 27031
[2008/06/20 10:56:26] INFO: [I=7(FLIPstx1)] MAD Port 27020
[2008/06/20 10:56:26] INFO: [I=8(FLIPlidder)] MAD Port 27023moverd vmoverd.html revision 65Black Box 2, port 3

[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] MAD Port 27031moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=7(FLIPstx1)] MAD Port 27020moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=8(FLIPlidder)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] MAD Port 27031moverd vmoverd.html revision 65Black Box 3, port 1
[2008/06/20 10:56:26] INFO: [I=7(FLIPstx1)] MAD Port 27020moverd vmoverd.html revision 65Black Box 2, port 0
[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=7(FLIPstx1)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=9(VALcytomat44)] MAD Server ready
[2008/06/20 10:56:26] INFO: [I=11(FLIPshaker1)] FLIPshaker1 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=12(VAlevolution)] VAlevolution Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=6(VALelx405)] VALelx405 Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=13(DeeracFLIP)] DeeracFLIP Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=10(VALenvision)] VALenvision Mover Administration Daemon
[2008/06/20 10:56:26] INFO: [I=11(FLIPshaker1)] MAD Port 27021
[2008/06/20 10:56:26] INFO: [I=6(VALelx405)] MAD Port 27012
[2008/06/20 10:56:26] INFO: [I=12(VAlevolution)] MAD Port 27030
[2008/06/20 10:56:26] INFO: [I=13(DeeracFLIP)] MAD Port 27010
[2008/06/20 10:56:26] INFO: [I=11(FLIPshaker1)] MAD Port 27021moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=6(VALelx405)] MAD Port 27012moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=12(VAlevolution)] MAD Port 27030moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=13(DeeracFLIP)] MAD Port 27010moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=11(FLIPshaker1)] MAD Port 27021moverd vmoverd.html revision 65Black Box 2, port 1
[2008/06/20 10:56:26] INFO: [I=10(VALenvision)] MAD Port 27001
[2008/06/20 10:56:26] INFO: [I=6(VALelx405)] MAD Port 27012moverd vmoverd.html revision 65Black Box 1, port 2
[2008/06/20 10:56:26] INFO: [I=12(VAlevolution)] MAD Port 27030moverd vmoverd.html revision 65Black Box 3, port 0
[2008/06/20 10:56:26] INFO: [I=13(DeeracFLIP)] MAD Port 27010moverd vmoverd.html revision 65Black Box 1, port 0
[2008/06/20 10:56:26] INFO: [I=10(VALenvision)] MAD Port 27001moverd vmoverd.html revision 65
[2008/06/20 10:56:26] INFO: [I=11(FLIPshaker1)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=6(VALelx405)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=12(VAlevolution)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=13(DeeracFLIP)] Simulation mode is disabled
[2008/06/20 10:56:26] INFO: [I=10(VALenvision)] MAD Port 27001moverd vmoverd.html revision 65Black Box 0, port 1
[2008/06/20 10:56:26] INFO: [I=10(VALenvision)] Simulation mode is disabled
[2008/06/20 10:56:27] INFO: [I=8(FLIPlidder)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=2(FLIPFlexdrop1)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=7(FLIPstx1)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=4(FLIPlpx1)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=11(FLIPshaker1)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=10(VALenvision)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=12(VAlevolution)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=3(FLIPFlexdrop2)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=6(VALelx405)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=13(DeeracFLIP)] MAD Server ready
[2008/06/20 10:56:27] INFO: [I=5(FLIPlpx2)] MAD Server ready
[2008/06/20 11:56:29] INFO: [I=32(Cytomat44)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:29] INFO: [I=33(sbcr)] ClassDescription="Thermo Shadow Bar Code Reader" Version=23.9.0 RL
[2008/06/20 11:56:30] INFO: [I=32(Cytomat44)] Instrument Mode from cfg file = -1

[2008/06/20 11:56:30] INFO: [I=34(LPX1)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:30] INFO: [I=33(sbcr)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:30] INFO: [I=35(LPX2)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:30] INFO: [I=32(Cytomat44)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=34(LPX1)] Instrument Mode from cfg file = -1
[2008/06/20 11:56:30] INFO: [I=36(Equator)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:30] INFO: [I=33(sbcr)] Instrument Mode from cfg file = -1
[2008/06/20 11:56:30] INFO: [I=35(LPX2)] Instrument Mode from cfg file = -1
[2008/06/20 11:56:30] INFO: [I=32(Cytomat44)] Instrument Mode is set to full run.
[2008/06/20 11:56:30] INFO: [I=34(LPX1)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=36(Equator)] Instrument Mode from cfg file = -1
[2008/06/20 11:56:30] INFO: [I=33(sbcr)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=35(LPX2)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=34(LPX1)] Instrument Mode is set to full run.
[2008/06/20 11:56:30] INFO: [I=36(Equator)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=33(sbcr)] Instrument Mode is set to full run.
[2008/06/20 11:56:30] INFO: [I=35(LPX2)] Instrument Mode is set to full run.
[2008/06/20 11:56:30] INFO: [I=36(Equator)] Instrument Mode is set to full run.
[2008/06/20 11:56:30] INFO: [I=0(?)] Instrument Mode from dictionary = 0
[2008/06/20 11:56:30] INFO: [I=0(?)] Instrument Mode from cfg file = -1
[2008/06/20 11:56:30] INFO: [I=0(?)] InstrumentMode set from dictionary
[2008/06/20 11:56:30] INFO: [I=0(?)] Instrument Mode is set to full run.
[2008/06/20 11:56:31] INFO: [I=30(lidder)] Initialization Successful. Instrument ID: 30.
[2008/06/20 11:56:31] INFO: [I=30(lidder)] Instrument Mode is = 0
[2008/06/20 11:56:36] INFO: [I=33(sbcr)] Instrument initialized.
[2008/06/20 11:57:13] INFO: [I=32(Cytomat44)] Instrument initialized.
[2008/06/20 11:57:34] INFO: [I=34(LPX1)] Instrument initialized.
[2008/06/20 11:57:45] INFO: [I=35(LPX2)] Instrument initialized.
[2008/06/20 11:57:46] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 1, start sample: 1, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=2:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 2, start sample: 2, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=3:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 3, start sample: 3, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=4:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 4, start sample: 4, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=5:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 5, start sample: 5, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=6:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 6, start sample: 6, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=7:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 7, start sample: 7, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=8:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 8, start sample: 8, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=9:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 9, start sample: 9, container: 1, num nests:
[2008/06/20 11:57:46] INFO: [S=10:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 10, start sample: 10, container: 1, num
[2008/06/20 11:57:46] INFO: [S=11:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 11, start sample: 11, container: 1, num
[2008/06/20 11:57:46] INFO: [S=12:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 12, start sample: 12, container: 1, num
[2008/06/20 11:57:46] INFO: [S=13:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 13, start sample: 13, container: 1, num

[2008/06/20 11:57:46] INFO: [S=14:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 14, start sample: 14, container: 1, num
[2008/06/20 11:57:46] INFO: [S=15:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 15, start sample: 15, container: 1, num
[2008/06/20 11:57:46] INFO: [S=16:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 16, start sample: 16, container: 1, num
[2008/06/20 11:57:46] INFO: [S=17:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 17, start sample: 17, container: 1, num
[2008/06/20 11:57:46] INFO: [S=18:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 18, start sample: 18, container: 1, num
[2008/06/20 11:57:46] INFO: [S=19:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 19, start sample: 19, container: 1, num
[2008/06/20 11:57:46] INFO: [S=20:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 20, start sample: 20, container: 1, num
[2008/06/20 11:57:46] INFO: [S=21:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 21, start sample: 21, container: 1, num
[2008/06/20 11:57:46] INFO: [S=22:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 22, start sample: 22, container: 1, num
[2008/06/20 11:57:46] INFO: [S=23:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 23, start sample: 23, container: 1, num
[2008/06/20 11:57:46] INFO: [S=24:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 24, start sample: 24, container: 1, num
[2008/06/20 11:57:46] INFO: [S=25:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 25, start sample: 25, container: 1, num
[2008/06/20 11:57:46] INFO: [S=26:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 26, start sample: 26, container: 1, num
[2008/06/20 11:57:46] INFO: [S=27:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 27, start sample: 27, container: 1, num
[2008/06/20 11:57:46] INFO: [S=28:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 28, start sample: 28, container: 1, num
[2008/06/20 11:57:46] INFO: [S=29:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 29, start sample: 29, container: 1, num
[2008/06/20 11:57:46] INFO: [S=30:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 30, start sample: 30, container: 1, num
[2008/06/20 11:57:46] INFO: [S=31:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 31, start sample: 31, container: 1, num
[2008/06/20 11:57:46] INFO: [S=32:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 32, start sample: 32, container: 1, num
[2008/06/20 11:57:46] INFO: [S=33:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 33, start sample: 33, container: 1, num
[2008/06/20 11:57:46] INFO: [S=34:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 34, start sample: 34, container: 1, num
[2008/06/20 11:57:46] INFO: [S=35:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 35, start sample: 35, container: 1, num
[2008/06/20 11:57:46] INFO: [S=36:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 36, start sample: 36, container: 1, num
[2008/06/20 11:57:46] INFO: [S=37:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 37, start sample: 37, container: 1, num
[2008/06/20 11:57:46] INFO: [S=38:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 38, start sample: 38, container: 1, num
[2008/06/20 11:57:46] INFO: [S=39:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 39, start sample: 39, container: 1, num
[2008/06/20 11:57:46] INFO: [S=40:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 40, start sample: 40, container: 1, num

[2008/06/20 11:57:46] INFO: [S=41:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 41, start sample: 41, container: 1, num
[2008/06/20 11:57:46] INFO: [S=42:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 42, start sample: 42, container: 1, num
[2008/06/20 11:57:46] INFO: [S=43:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 43, start sample: 43, container: 1, num
[2008/06/20 11:57:46] INFO: [S=44:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 44, start sample: 44, container 1, num
[2008/06/20 11:57:46] INFO: [S=45:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 45, start sample: 45, container: 1, num
[2008/06/20 11:57:46] INFO: [S=46:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 46, start sample: 46, container: 1, num
[2008/06/20 11:57:46] INFO: [S=47:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 47, start sample: 47, container: 1, num
[2008/06/20 11:57:46] INFO: [S=48:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 48, start sample: 48, container: 1, num
[2008/06/20 11:57:46] INFO: [S=49:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 49, start sample: 49, container: 1, num
[2008/06/20 11:57:46] INFO: [S=50:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 50, start sample: 50, container: 1, num
[2008/06/20 11:57:46] INFO: [S=51:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 51, start sample: 51, container: 1, num
[2008/06/20 11:57:46] INFO: [S=52:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 52, start sample: 52, container: 1, num
[2008/06/20 11:57:46] INFO: [S=53:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 53, start sample: 53, container: 1, num
[2008/06/20 11:57:46] INFO: [S=54:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 54, start sample: 54, container: 1, num
[2008/06/20 11:57:46] INFO: [S=55:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 55, start sample: 55, container: 1, num
[2008/06/20 11:57:46] INFO: [S=56:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 56, start sample: 56, container: 1, num
[2008/06/20 11:57:46] INFO: [S=57:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 57, start sample: 57, container: 1, num
[2008/06/20 11:57:46] INFO: [S=58:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 58, start sample: 58, container: 1, num
[2008/06/20 11:57:46] INFO: [S=59:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 59, start sample: 59, container: 1, num
[2008/06/20 11:57:46] INFO: [S=60:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 60, start sample: 60, container: 1, num
[2008/06/20 11:57:46] INFO: [S=61:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 61, start sample: 61, container: 1, num
[2008/06/20 11:57:46] INFO: [S=62:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 62, start sample: 62, container: 1, num
[2008/06/20 11:57:46] INFO: [S=63:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 63, start sample: 63, container: 1, num
[2008/06/20 11:57:46] INFO: [S=64:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 64, start sample: 64, container: 1, num
[2008/06/20 11:57:46] INFO: [S=65:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 65, start sample: 65, container: 1, num
[2008/06/20 11:57:46] INFO: [S=66:C=1(A_COMPOUND):I=35(LPX2)] Adding containers: start nest: 66, start sample: 66, container: 1, num
[2008/06/20 11:57:46] INFO: [] Sequence started; T = 0.
[2008/06/20 11:57:53] INFO: [] continuing run after 0 seconds of slip.
[2008/06/20 11:57:54] INFO: [] Total slip time 0 relative time 1

[2008/06/20 11:57:56] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=1:M=2] STARTING PrepareNestForGet
[2008/06/20 11:57:56] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=1:M=2] SCHEDULED START TIME: 0
[2008/06/20 11:57:56 - 2008/06/20 11:58:12] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=1:M=2] DONE PrepareNestForGet
[2008/06/20 11:58:14] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=2:M=2] STARTING PGet
[2008/06/20 11:58:14] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=2:M=2] SCHEDULED START TIME: 20
[2008/06/20 10:58:14] INFO: [I=5(FLIPlpx2)] Set grip offset to 0 (was 9999)
[2008/06/20 11:58:14 - 2008/06/20 11:58:18] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=2:M=2] DONE PGet
[2008/06/20 11:58:18] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=3:M=2] STARTING BeltPut
[2008/06/20 11:58:18 - 2008/06/20 11:58:20] INFO: [S=1:C=1(A_COMPOUND):I=35(LPX2):Q=3:M=2] DONE BeltPut
[2008/06/20 10:58:20] INFO: [S=1:C=1(A_COMPOUND):I=1(belt):Q=4:M=2] STARTING Convey
[2008/06/20 10:58:20 - 2008/06/20 10:58:20] INFO: [S=1:C=1(A_COMPOUND):I=1(belt):Q=4:M=2] DONE Convey
[2008/06/20 11:58:20] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=5:M=2] STARTING BeltGet
[2008/06/20 11:58:20] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=5:M=2] SCHEDULED START TIME: 27
[2008/06/20 10:58:20] INFO: [I=13(DeeracFLIP)] Set grip offset to 0 (was 9999)
[2008/06/20 11:58:20 - 2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=5:M=2] DONE BeltGet
[2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=6:M=2] STARTING CompletePut
[2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=6:M=2] SCHEDULED START TIME: 33
[2008/06/20 11:58:30 - 2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=6:M=2] DONE CompletePut
[2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=7:M=2] STARTING RunProgram
[2008/06/20 11:58:30] INFO: [S=1:C=1(A_COMPOUND):I=36(Equator):Q=7:M=2] SCHEDULED START TIME: 37

APPENDIX-D

Automation-generated error log for a shortened run

Start Time: 2008/04/24 17:18:19

Run Errors Start:

Date	Time	Sample	Container	Instrument	Type	Message
2008/04/24	18:26:37	NA	NA	VAL1	INTERVENE	Failed to put to nest "VPREP_1:nest[1]". (Count=1) Reported MoverD Error :axis 3, moving error, holding error, motor shutdown
2008/04/24	18:50:47	NA	NA	VAL1	INTERVENE	Move to safe failed: unknown start point:unknown start point
2008/04/24	18:56:28	NA	NA	VAL1	WARNING	Recover retry failed: retry failed
2008/04/24	18:56:31	NA	NA	VAL1	INTERVENE	Ensure that ALL movers are clear. Could not initiate PrepareToStore, mover error: illegal command in recovery mode
2008/04/24	18:58:37	NA	NA	VAL1	INTERVENE	Get from nest VPREP_1:nest[1] failed. (Count=1) :missing plate
2008/04/24	19:06:32	NA	NA	VAL1	INTERVENE	Get from nest VPREP_1:nest[1] failed. (Count=2) :missing plate
2008/04/24	19:07:55	NA	NA	VAL1	INTERVENE	Get from nest VPREP_1:nest[2] failed. (Count=1) :missing plate
2008/04/24	19:11:15	12	2	Teleshake	INTERVENE	
2008/04/24	19:12:15	12	2	Teleshake	INTERVENE	
2008/04/24	19:13:15	12	2	Teleshake	INTERVENE	
2008/04/24	19:14:33	NA	NA	Teleshake	FATAL	User aborted the run!